Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1617SXK

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS	4	OCT 28	KOREAPAT now available on STN
NEWS	5	NOV 30	PHAR reloaded with additional data
NEWS	6	DEC 01	LISA now available on STN
NEWS	7	DEC 09	12 databases to be removed from STN on December 31, 2004
NEWS	8	DEC 15	MEDLINE update schedule for December 2004
NEWS	9	DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	10	DEC 17	COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	11	DEC 17	SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	12	DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13	DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS	14	DEC 30	EPFULL: New patent full text database to be available on STN
NEWS	15	DEC 30	CAPLUS - PATENT COVERAGE EXPANDED
NEWS	16	JAN 03	No connect-hour charges in EPFULL during January and February 2005
NEWS	17	FEB 25	CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS	18	FEB 10	STN Patent Forums to be held in March 2005
NEWS	19	FEB 16	STN User Update to be held in conjunction with the 229th ACS National Meeting on March 13, 2005
NEWS	20	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	21	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	22	FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	23	MAR 02	GBFULL: New full-text patent database on STN
NEWS	24	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	25	MAR 03	MEDLINE file segment of TOXCENTER reloaded

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:05:25 ON 21 MAR 2005

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'CAPLUS' ENTERED AT 14:05:35 ON 21 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 21 Mar 2005 VOL 142 ISS 13
FILE LAST UPDATED: 20 Mar 2005 (20050320/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s flavonoid?
L1 30430 FLAVONOID?

=> e flavonoid?
E1 20474 FLAVONOID/BI
E2 2 FLAVONOID3/BI
E3 0 --> FLAVONOID?/BI
E4 78 FLAVONOIDAL/BI
E5 1 FLAVONOIDCONTENT/BI
E6 6 FLAVONOIDE/BI
E7 1 FLAVONOIDEN/BI
E8 40 FLAVONOIDES/BI
E9 1 FLAVONOIDGLYCOSIDE/BI
E10 1 FLAVONOIDGLYCOSIDES/BI
E11 18 FLAVONOIDIC/BI
E12 1 FLAVONOIDINHIBITING/BI

=> s chemotherapeutic agetns
17306 CHEMOTHERAPEUTIC
1698 CHEMOTHERAPEUTICS
18613 CHEMOTHERAPEUTIC (CHEMOTHERAPEUTIC OR CHEMOTHERAPEUTICS)
1 AGETNS
L2 0 CHEMOTHERAPEUTIC AGETNS (CHEMOTHERAPEUTIC(W)AGETNS)

```
=> s chemotherapeutic agent?
         17306 CHEMOTHERAPEUTIC
          1698 CHEMOTHERAPEUTICS
         18613 CHEMOTHERAPEUTIC
                 (CHEMOTHERAPEUTIC OR CHEMOTHERAPEUTICS)
       1459504 AGENT?
L3        8561 CHEMOTHERAPEUTIC AGENT?
                 (CHEMOTHERAPEUTIC(W)AGENT?)

=> s L1 and L3
L4          27 L1 AND L3

=> dup rem
ENTER L# LIST OR (END):L4
PROCESSING COMPLETED FOR L4
L5           27 DUP REM L4 (0 DUPLICATES REMOVED)

=> d 1-24 IBIB ABS

L5   ANSWER 1 OF 27  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:        2005:226330  CAPLUS
TITLE:                   Apigenin inhibits VEGF and HIF-1 expression via
                         PI3K/AKT/p70s6K1 and HDM2/p53 pathways
AUTHOR(S):               Fang, Jing; Xia, Chang; Cao, Zongxian; Zheng, Jenny
                         Z.; Reed, Eddie; Jiang, Bing-Hua
CORPORATE SOURCE:        The Mary Babb Randolph Cancer Center, Department of
                         Microbiology, Immunology and Cell Biology, West
                         Virginia University, Morgantown, WV, 26506-9300, USA
SOURCE:                  FASEB Journal (2005), 19(3), 342-353
                         CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER:               Federation of American Societies for Experimental
                         Biology
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Apigenin is a nontoxic dietary flavonoid that has been shown to
     possess anti-tumor properties and therefore poses special interest for the
     development of a novel chemopreventive and/or chemotherapeutic
     agent for cancer. Ovarian cancer is one of the most common causes
     of cancer death among women. Here we demonstrate that apigenin inhibits
     expression of vascular endothelial growth factor (VEGF) in human ovarian
     cancer cells. VEGF plays an important role in tumor angiogenesis and
     growth. We found that apigenin inhibited VEGF expression at the
     transcriptional level through expression of hypoxia-inducible factor lot
     (HIF-lot). Apigenin inhibited expression of HIF-lot and VEGF via the
     PI3K/AKT/p70S6K1 and HDM2/p53 pathways. Apigenin inhibited tube formation
     in vitro by endothelial cells. These findings reveal a novel role of
     apigenin in inhibiting HIF-1 and VEGF expression that is important for
     tumor angiogenesis and growth, identifying new signaling mols. that
     mediate this regulation.

L5   ANSWER 2 OF 27  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:        2005:15059  CAPLUS
DOCUMENT NUMBER:         142:169994
TITLE:                   Curcumin induces glutathione biosynthesis and inhibits
                         NF-κB activation and interleukin-8 release in
                         alveolar epithelial cells: Mechanism of free radical
                         scavenging activity
AUTHOR(S):               Biswas, Saibal K.; McClure, Danny; Jimenez, Luis A.;
                         Megson, Ian L.; Rahman, Irfan
CORPORATE SOURCE:        Centre for Cardiovascular Sciences, School of
                         Biomedical and Clinical Laboratory Sciences, Medical
                         School, University of Edinburgh, Edinburgh, UK
SOURCE:                  Antioxidants & Redox Signaling (2005), 7(1 & 2), 32-41
                         CODEN: ARSIF2; ISSN: 1523-0864
```

PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Oxidants and tumor necrosis factor-α (TNF-α) activate transcription factors such as nuclear factor-κB (NF-κB), which is involved in the transcription of proinflammatory mediators, including interleukin 8 (IL-8). Curcumin (diferuloylmethane) is a naturally occurring **flavonoid** present in the spice turmeric, which has a long traditional use as a **chemotherapeutic agent** for many diseases. We hypothesize that curcumin may possess both antioxidant and antiinflammatory properties by increasing the glutathione levels and inhibiting oxidant- and cytokine-induced NF-κB activation and IL-8 release from cultured alveolar epithelial cells (A549). Treatment of A549 cells with hydrogen peroxide (H2O2; 100 μM) and TNF-α (10 ng/mL) significantly increased NF-κB and activator protein-1 (AP-1) activation, as well as IL-8 release. Curcumin inhibited both H2O2- and TNF-α-mediated activation of NF-κB and AP-1, and IL-8 release. Furthermore, an increased level of GSH and glutamylcysteine ligase catalytic subunit mRNA expression was observed in curcumin-treated cells as compared with untreated cells. Curcumin interacted directly with superoxide anion (O2.-) and hydroxyl radical (.OH) as shown by ESR, quenching the interaction of the radicals with the spin trap, Tempone-H. This suggests that curcumin has multiple properties: as an oxygen radical scavenger, antioxidant through modulation of glutathione levels, and antiinflammatory agent through inhibition of IL-8 release in lung cells.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:578807 CAPLUS
DOCUMENT NUMBER: 142:148584
TITLE: The **flavonoid** effect against vinblastine, cyclophosphamide and paracetamol toxicity by inhibition of lipid-peroxidation and increasing liver glutathione concentration
AUTHOR(S): Lahouel, M.; Boulkour, S.; Segueni, N.; Fillastre, J. P.
CORPORATE SOURCE: Laboratoire de Pharmacologie et Phytochimie, Departement de Biologie, Universite de Jijel, Jijel, 18000, Algeria
SOURCE: Pathologie Biologie (2004), 52(6), 314-322
CODEN: PTBIAN; ISSN: 0369-8114
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: French
AB The paracetamol and cyclophosphamide are metabolized in the liver by the cytochrome P 450. The formed reactive intermediates are responsible of a hepatocyte depletion of the glutathione and a lipoperoxidn. the vinblastine is also a **chemotherapeutic agent** hepatotoxic and hepatotoxic. Otherwise, **flavonoids** are polyphenols substances of plant origin having some biol. and anti-oxidative properties. However no information is available on their effects on glutathione and glutathione-s-transferases. In our research, we valued the effect of oral administration of **flavonoids** (diosmine and quercetine) under shape of propolis extract to 60 mg/kg daily during 14 days, on hematol. and hepatic toxicity of a single dose of cyclophosphamide 80 mg/kg by i.v. way, vinblastine 2 mg/kg by i.v. way and the hepatic toxicity of the paracetamol managed by oral way to 200 mg/kg corresponding to 2/3 the DL50 at the rat female albinos wistar. We did a blood numeration, an assessment of serum activities of transaminases and alkali phosphatases as well as quantification of the glutathione and the malondialdehyde (MDA) in liver homogenates of rats treated. Analyses are done at regular intervals; 1, 3, 7 and 14 days after the administration of drugs. In the group of rats treated by the cyclophosphamide paracetamol

alone we observed since the 1st day, an increase of lipid peroxide (MDA) of 120% and a downfall of hepatic glutathione including the group receiving the vinblastine (until 210% of reduction). In the same way a severe leucopenia and a thrombopenia (70% of reduction) are observed between the 3rd and the 14th day at rats treated by the **chemotherapeutic** agents alone (cyclophosphamide and vinblastine). The combination of flavonoids with drugs have clearly reduced the effect of drugs toxicity. Indeed, the aphasic observed with the vinblastine, as well as the leucopenia and thrombopenia of the cyclophosphamide are corrected entirely. In the same way, we noted a restoration of rates of peroxide and glutathione. **Flavonoids** seem to act by activation of the turn over of the glutathione and enzymes stimulating particularly glutathione-s-transferases permitting the captation of the reactive metabolites of the studied drugs.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:760087 CAPLUS
DOCUMENT NUMBER: 142:86047
TITLE: Role of **flavonoids** in the prevention of haematotoxicity due to **chemotherapeutic agents**
AUTHOR(S): Lahouel, Mesbah; Fillastre, Jean Paul
CORPORATE SOURCE: Laboratory of Pharmacology and Phytochemistry, Department of Biology, University of Jijel, Jijel, 18000, Algeria
SOURCE: Haema (2004), 7(3), 313-320
CODEN: HAGAB8; ISSN: 1108-2682
PUBLISHER: Epsilon
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Flavonoids** are polyphenols widely distributed and known to possess biol. and pharmacol. activities, including anti-inflammatory action against free radicals. Haematotoxicity is the main side-effect of **chemotherapeutic agents**. Therefore, the protection of chemotherapy toxicity by **flavonoids** is a new field in tumor therapy. Our study shows that oral administration of 100 mg/kg/daily over two weeks of **flavonoids** (diosmin, hesperidin, quercetin extracted from propolis and daflon) before chemotherapy injection offers some protection against the haematotoxicity of doxorubicin (DOX), cyclophosphamide (CPM) or daunorubicin (DNR). Female wistar rats were injected with a single dose of 10 mg/kg ADR, 40 mg/kg DNR or were given 100 mg/kg CPM in a single dose. A second group received **flavonoids** 100 mg/kg/daily before chemotherapy for two weeks. Blood samples were taken at different times: 3, 7, 14 and 28 days after the administration of **chemotherapeutic agents**. A haematol. depletion was observed following treatment with all chemotherapy agents alone, in the first group of rats. The leukopoenia reached the level of 1.500 cells/μl on day 2, and anemia presented three weeks after treatment. A significant protection of chemotherapy haematotoxicity occurred after pre-treatment with **flavonoids** 100 mg/kg in all groups. We observed no significant difference between rats receiving the combination of **flavonoids** and chemotherapy and control group. These results suggest that **flavonoids** seem to offer protection against chemotherapy toxicity.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:1008726 CAPLUS
DOCUMENT NUMBER: 142:68564
TITLE: Xanthohumol, a novel anti-HIV-1 agent purified from

hops Humulus lupulus

AUTHOR(S): Wang, Qian; Ding, Zhi-Hui; Liu, Ji-Kai; Zheng, Yong-Tang

CORPORATE SOURCE: Laboratory of Molecular Immunopharmacology, Kunming Institute of Zoology, Graduate School, Chinese Academy of Sciences, Kunming, 650223, Peop. Rep. China

SOURCE: Antiviral Research (2004), 64(3), 189-194
CODEN: ARSPDR; ISSN: 0166-3542

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Xanthohumol, prenylchacone **flavonoid**, is a natural product with multi-biofunctions purified from Hops Humulus lupulus. Its anti-HIV-1 activity was tested in the present study. Results showed that xanthohumol inhibited HIV-1 induced cytopathic effects, the production of viral p24 antigen and reverse transcriptase in C8166 lymphocytes at non-cytotoxic concentration The EC50 values were 0.82, 1.28, and 0.50 μg/mL, resp. The therapeutic index (TI) was about 10.8. Xanthohumol also inhibited HIV-1 replication in PBMC with EC50 value of 20.74 μg/mL. The activity of recombinant HIV-1 reverse transcriptase and the HIV-1 entry were not inhibited by xanthohumol. The results from this study suggested that xanthohumol is effective against HIV-1 and might serve as an interesting lead compound It may represent a novel **chemotherapeutic agent** for HIV-1 infection. However, the mechanism of its anti-HIV-1 effect needs to be further clarified.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:211283 CAPLUS

DOCUMENT NUMBER: 141:235838

TITLE: Protective effect of **flavonoids** against the toxicity of vinblastine, cyclophosphamide and paracetamol by inhibition of lipid-peroxidation and increase of liver glutathion

AUTHOR(S): Lahouel, Mesbah; Boulkour, Soraya; Segueni, Narimane; Fillastre, Jean Paul

CORPORATE SOURCE: Laboratory of Pharmacology and Phytochemistry, Department of Biology, University of Jijel, Jijel, 18000, Algeria

SOURCE: Haema (2004), 7(1), 59-67
CODEN: HAGAB8; ISSN: 1108-2682

PUBLISHER: Epsilon

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Paracetamol and cyclophosphamide are metabolized in the liver by the cytochrome P 450. The produced reactive intermediates are responsible for hepatocyte depletion of glutathione and for lipoperoxidn. Vinblastine is a **chemotherapeutic agent**, which is also hepatotoxic and hematotoxic. **Flavonoids** are polyphenols, substances of plant origin, having biol. and anti-oxidative properties. There is no available information for the effect of **flavonoids** on glutathione and glutathione-s-transferases. In our research, we evaluated the effect of oral administration of **flavonoids** (diosmine and quercetine; 60 mg/kg daily for 14 days) on hematol. and hepatic toxicity of a single dose of cyclophosphamide (80 mg/kg, IV), and vinblastine (2 mg/kg, IV), as well as on the hepatic toxicity of paracetamol given to rats. We measured a full blood count, serum levels of transaminases and alkaline phosphatase as well as levels of glutathione and malondialdehyde (MDA) in liver homogenates of the rats treated. Analyses were performed at regular intervals: 1, 3, 7 and 14 days after the administration of drugs. In the group of rats treated by cyclophosphamide or paracetamol alone, an increase of lipid peroxide (MDA) of 120% and a reduction of hepatic glutathione were observed These changes started after the first day of

treatment. Severe leucopenia and thrombocytopenia (70% of reduction) were also observed between the 3rd and the 14th day in rats treated with the **chemotherapeutic agents** alone (cyclophosphamide or vinblastine). The combination of **flavonoids** and chemotherapy produced a clear reduction of drugs toxicity. Bone marrow aplasia, leucopenia and thrombocytopenia were corrected entirely. Furthermore, a restoration of peroxide and glutathione was also observed. Flavonoids seem to act by the activation of glutathione turnover and enzymes that stimulate particularly glutathione-s-transferases, which permit the capitation of the reactive metabolites of the studied drugs.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:486847 CAPLUS
DOCUMENT NUMBER: 141:46900
TITLE: Inhibition of cyclooxygenase-2 activity in head and neck cancer cells by genistein
AUTHOR(S): Ye, Fei; Wu, Josephine; Dunn, Trish; Yi, Jizu; Tong, Xiaodi; Zhang, David
CORPORATE SOURCE: Department of Pathology, Mount Sinai School of Medicine, New York University, New York, NY, 10029NY, USA
SOURCE: Cancer Letters (Amsterdam, Netherlands) (2004), 211(1), 39-46
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Genistein, rich in soybean, has been reported to have anti-cancer activity on several cancers. However, the mol. mechanism of its anti-cancer activity still remains unclear. We investigated the effect of genistein on a human oral squamous carcinoma line (SCC-25), and demonstrated that genistein inhibited SCC-25 cell growth via G2/M phase arrest. We observed a significant decrease of proliferating cell nuclear antigen expression in these cells after treatment, but no significant change in the number of apoptotic cells, indicating that the major action of genistein is inhibition of cancer cell proliferation. We also observed a high level of prostaglandin E2 (PGE2) in these cells and PGE2 synthesis in SCC-25 cells was significantly suppressed by genistein. We demonstrated that genistein directly inhibited cyclooxygenase-2 (COX-2) activity, an inducible enzyme that converts arachidonic acid to prostaglandins, similar to the action of celecoxib, a selective COX-2 inhibitor. However, the anticancer activity of genistein was much weaker than that of indomethacin (non-selective COX inhibitor), celecoxib and baicalein (flavonoid isolated from Scutellaria baicalensis). These results suggested that genistein might be useful as a chemopreventive agent rather than a **chemotherapeutic agent**.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:557093 CAPLUS
DOCUMENT NUMBER: 139:390885
TITLE: Inhibition of Cancer Cell Proliferation and Prostaglandin E2 Synthesis by Scutellaria Baicalensis
AUTHOR(S): Zhang, David Y.; Wu, Josephine; Ye, Fei; Xue, Li; Jiang, Shiquan; Yi, Jizu; Zhang, Wandi; Wei, Huachen; Sung, Max; Wang, Wayne; Li, Xiaoping
CORPORATE SOURCE: Department of Pathology, Mount Sinai School of Medicine, New York, NY, 10029, USA
SOURCE: Cancer Research (2003), 63(14), 4037-4043
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Scutellaria baicalensis is a widely used Chinese herbal medicine that has been used historically in anti-inflammatory and anticancer therapy. The purpose of this study is to verify its anticancer activity on head and neck squamous cell carcinoma (HNSCC) in vitro and in vivo and to investigate its effect on cyclooxygenase 2 (COX 2), which converts arachidonic acid to prostaglandin E2 (PGE2) and is highly expressed in HNSCC. Two human HNSCC cell lines (SCC-25 and KB) and a nontumorigenic cell line (HaCaT) were tested in vitro for growth inhibition, proliferation cell nuclear antigen expression, and COX-2 activity and expression after treatment with Scutellaria baicalensis extract Its effects were compared with those of baicalein (a **flavonoid** isolated from Scutellaria baicalensis), indomethacin (a nonselective COX inhibitor), and celecoxib (a selective COX-2 inhibitor). Four nude mice with s.c. inoculation of KB cells were tested for its anticancer activity in vivo by oral administration of Scutellaria baicalensis at a dose of 1.5 mg/mouse (75 mg/kg), five times/wk for 7 wk. Scutellaria baicalensis and other agents demonstrated a strong growth inhibition in both tested human HNSCC cell lines. No growth inhibition of HaCaT cells was observed with Scutellaria baicalensis. The IC50s were 150 μg/mL for Scutellaria baicalensis, 25 μM for celecoxib, and 75 μM for baicalein and indomethacin. Scutellaria baicalensis, as well as celecoxib and indomethacin, but not baicalein, suppressed proliferation cell nuclear antigen expression and PGE2 synthesis in both cell types. Scutellaria baicalensis inhibited COX-2 expression, whereas celecoxib inhibited COX-2 activity directly. A 66% reduction in tumor mass was observed in the nude mice.

Scutellaria baicalensis selectively and effectively inhibits cancer cell growth in vitro and in vivo and can be an effective **chemotherapeutic agent** for HNSCC. Inhibition of PGE2 synthesis via suppression of COX-2 expression may be responsible for its anticancer activity. Differences in biol. effects of Scutellaria baicalensis compared with baicalein suggest the synergistic effects among components in Scutellaria baicalensis.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:198491 CAPLUS
DOCUMENT NUMBER: 139:223762
TITLE: Baicalein and baicalin as inhibitors of HIV-1 integrase
AUTHOR(S): Lee, Min Jun; Kim, Mira; Lee, Yong Sup; Shin, Cha-Gyun
CORPORATE SOURCE: Department of Biotechnology, Chung-Ang University, Ansung, Kyungki, 456-756, S. Korea
SOURCE: Yakhak Hoechi (2003), 47(1), 46-51
CODEN: YAHOA3; ISSN: 0513-4234
PUBLISHER: Pharmaceutical Society of Korea
DOCUMENT TYPE: Journal
LANGUAGE: Korean

AB Baicalein and baicalin are **flavonoid** compds. isolated from medicinal herb Scutellaria baicalensis Georgi (Labiatae) and have been known to possess antiviral activities. In the present study, we investigated the in vitro effects of baicalein and baicalin on the three distinctive enzymic activities of the human immunodeficiency virus type-1 (HIV-1) integrase - endonucleolytic, integration, and disintegration activities. Both compds. inhibited the three enzymic activities in a dose-dependent manner. The 50% inhibitory concns. of baicalein and baicalin for endonucleolytic activities of HIV-1 integrase were 4.4±3.3 and 25.9±4.0 μM, resp. In general, baicalein exhibited nearly 6- to 10-fold stronger inhibition than baicalin for the three enzymic activities. These data demonstrate that baicalein or baicalin can be used as a leading compound to develop anti-AIDS **chemotherapeutic**

agents targeting to the HIV-1 integrase.

L5 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:526480 CAPLUS
DOCUMENT NUMBER: 138:117325
TITLE: High-throughput measurement of the Tp53 response to anticancer drugs and random compounds using a stably integrated
AUTHOR(S): Sohn, Taylor A.; Bansal, Ravi; Su, Gloria H.; Murphy, Kathleen M.; Kern, Scott E.
CORPORATE SOURCE: Department of Surgery, The Johns Hopkins Medical Institutions, Baltimore, MD, USA
SOURCE: Carcinogenesis (2002), 23(6), 949-957
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human Tp53 is normally a short-lived protein. Tp53 protein is stabilized and levels are increased in response to a variety of cellular stresses, including those induced by genotoxic anticancer drugs and environmental exposures. To engineer an efficient assay based on this property, we constructed and integrated a Tp53-specific reporter system into human cancer cells, termed p53R cells. We tested a range of conventional **chemotherapeutic agents** as well as over 16 000 diverse small compds. Ionizing radiation and two-thirds of conventional **chemotherapeutic agents**, but only 0.2% of diverse compds. activated Tp53 activity by two-fold or greater, consistent with the presumptive genotoxic activation of Tp53 function. Cytotoxicity was independent of TP53 genetic status when paired, syngeneic wild-type TP53 and TP53-null cells in culture were treated with compds. that activated Tp53. From the unbiased survey of random compds., Tp53 activation was strongly induced by an analog of AMSA, an investigational anti-cancer agent. Tp53 was also strongly induced by an N-oxide of quinoline and by dabequine, an exptl. antimalarial evaluated in humans; dabequine was reported to be neg. in other screens of mutagenicity and clastogenicity but carcinogenic in animal studies. Further exploration of antimalarial compds. identified the common medicinals chloroquine, quinacrine, and amodiaquine as Tp53-inducers. **Flavonoids** are known to have DNA topoisomerase activity, a Tp53-inducing activity that is confirmed in the assay. A reported clin. association of Tp53 immunopos. colorectal cancers with use of the antihypertensive agents was extended by the demonstration of hydralazine and nifedipine as Tp53-inducers. P53R cells represent an efficient Tp53 functional assay to identify chems. and other agents with interesting biol. properties, including genotoxicity. This assay may have utility in the identification of novel chemotherapeutic **agents**, as an adjunct in the pharmaceutical optimization of lead compds., in the exploration of environmental exposures, and in chemical probing of the Tp53 pathway.
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:461862 CAPLUS
DOCUMENT NUMBER: 138:49527
TITLE: Effects of luteolin on the inhibition of proliferation and induction of apoptosis in human myeloid leukaemia cells
AUTHOR(S): Ko, W. G.; Kang, T. H.; Lee, S. J.; Kim, Y. C.; Lee, B. H.
CORPORATE SOURCE: College of Pharmacy and Medicinal Resources Research Center, Wonkwang University, Jeonbuk, 570-749, S. Korea
SOURCE: Phytotherapy Research (2002), 16(3), 295-298
CODEN: PHYREH; ISSN: 0951-418X

PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Luteolin, a **flavonoid** isolated from the fruit of Vitex rotundifolia, has been examined with regard to the inhibition of proliferation and induction of apoptosis in human myeloid leukemia HL-60 cells. The concentration required for 50% inhibition of the growth after 96 h was 15±1.1 μM. The mode of cell death induced by luteolin was found to be apoptosis, as judged by the morphol. alteration of the cells and by the detection of DNA fragmentation using agarose gel electrophoresis. The degree of apoptosis was quantified by a sandwich enzyme immunoassay and flow cytometric anal. These results suggest that luteolin may be used as potential chemopreventive and **chemotherapeutic agents**.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:190371 CAPLUS
TITLE: Preclinical and clinical development of cdk inhibitors
AUTHOR(S): Senderowicz, Adrian M.
CORPORATE SOURCE: Molecular Therapeutics Unit, Oral Pharyngeal Cancer Branch, NIH, Bethesda, MD, 20892-4340, USA
SOURCE: Abstracts of Papers, 223rd ACS National Meeting, Orlando, FL, United States, April 7-11, 2002 (2002), MEDI-252. American Chemical Society: Washington, D. C.
CODEN: 69CKQP
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Flavopiridol (NSC 649890, HMR 1275) is a **flavonoid** with potent CDK inhibitory activity. In preclin. models of lymphoid and head and neck cancers, flavopiridol induced apoptosis irresp. of the presence of BCL-2 or p53. The first Phase 1 trial of a cdk inhibitor, flavopiridol, has been completed. The main side effects noted were secretory diarrhea and pro-inflammatory syndrome, while antitumor activity was observed in several tumor types. Concns. between 300 and 500 nM-necessary to inhibit CDK and achieve an antiproliferative effect-were achieved safely. Phase 2 trials with infusional flavopiridol and Phase I infusional trials in combination with standard **chemotherapeutic agents** are being completed. Another cdk modulator, UCN-01 (7-hydroxystaurosporine; NSC 638850), has also been entered in clin. trials. These first two CDK modulators have shown encouraging results in early clin. trials; the best schedule to be administered and best combination strategies are still under investigation.

L5 ANSWER 13 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:725074 CAPLUS
DOCUMENT NUMBER: 138:264985
TITLE: Antioxidant nutrients and adriamycin toxicity
AUTHOR(S): Quiles, Jose L.; Huertas, Jesus R.; Battino, Maurizio; Mataix, Jose; Ramirez-Tortosa, M. Carmen
CORPORATE SOURCE: Institute of Nutrition and Food Technology, Department of Physiology, University of Granada, Granada, 18071, Spain
SOURCE: Toxicology (2002), 180(1), 79-95
CODEN: TXCYAC; ISSN: 0300-483X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The anthracycline antibiotic adriamycin (doxorubicin) is one of the most effective **chemotherapeutic agents** against a wide variety of cancers. However, its use is seriously limited by the development in the heart of acute and chronic toxic effects. Mechanisms of action and toxicity of adriamycin are briefly revised in this review.

Among followed strategies to attenuate adriamycin toxicity are dosage optimization, synthesis and use of analogs or combined therapy with antioxidants. The most promising results come from the combination of the drug delivery together with an antioxidant to reduce oxidative stress. Many antioxidants have been assayed with very different results. Among these mols., metal ions chelators and low-mol.-mass agents that scavenge reactive oxygen species and that are synthesized in vivo have been widely studied. However, the present review will be exclusively focused on the antioxidants that are derived from the diet, in particular the role of vitamin E, vitamin C, vitamin A, coenzyme Q, ~~flavonoids,~~ antioxidant components of virgin olive oil and selenium.

REFERENCE COUNT: 143 THERE ARE 143 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:709408 CAPLUS
DOCUMENT NUMBER: 136:95670
TITLE: Selective Growth-Inhibitory, Cell-Cycle Deregulatory and Apoptotic Response of Apigenin in Normal versus Human Prostate Carcinoma Cells
AUTHOR(S): Gupta, Sanjay; Afaq, Farrukh; Mukhtar, Hasan
CORPORATE SOURCE: Department of Dermatology, Case Western Reserve University and Research Institute of University Hospitals of Cleveland, Cleveland, OH, 44106, USA
SOURCE: Biochemical and Biophysical Research Communications (2001), 287(4), 914-920
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Agents that are capable of inducing selective apoptosis of cancer cells are receiving considerable attention in developing novel cancer-preventive approaches. In the present study, employing normal human prostate epithelial cells (NHPE), virally transformed normal human prostate epithelial cells (PZ-HPV-7), and human prostate adenocarcinoma (CA-HPV-10) cells, we evaluated the growth-inhibitory effects of apigenin, a flavonoid abundantly present in fruits and vegetables. Apigenin treatment to NHPE and PZ-HPV-7 resulted in almost similar growth inhibitory responses of low magnitude. In sharp contrast, apigenin treatment resulted in a significant decrease in cell viability of CA-HPV-10 cells. Similar selective growth inhibitory effects were also observed for human epidermoid carcinoma A431 cells compared to normal human epidermal keratinocytes. Apigenin treatment resulted in significant apoptosis of CA-HPV-10 cells as evident from (i) DNA ladder assay, (ii) fluorescence microscopy, and (iii) TUNEL assay, whereas the NHPE and PZ-HPV-7 cells did not undergo apoptosis but showed exclusive necrotic staining only at a high dose of 40 μM. Apigenin (1-10 μM) also resulted in a dose-dependent G2-M phase cell cycle arrest of CA-HPV-10 cells but not of PZ-HPV-7 cells. The growth-inhibitory and apoptotic potential of apigenin was also observed in a variety of prostate carcinoma cells representing different stage and androgen responsiveness. Apigenin may be developed as a promising chemopreventive and/or **chemotherapeutic agent** against prostate cancer. (c) 2001 Academic Press.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:216235 CAPLUS
DOCUMENT NUMBER: 135:269
TITLE: Quercetin inhibits the expression and function of the androgen receptor in LNCaP prostate cancer cells
AUTHOR(S): Xing, Nianzeng; Chen, Yi; Mitchell, Susan H.; Young,

Charles Y. F.
CORPORATE SOURCE: Department of Urology and Biochemistry and Molecular Biology, Mayo Graduate School, Mayo Foundation, Rochester, MN, 55905, USA
SOURCE: Carcinogenesis (2001), 22(3), 409-414
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The androgen receptor (AR) is involved in the development and progression of prostate cancer. In order to find new compds. that may present novel mechanisms to attenuate the function of AR, we investigated the effect of a natural **flavonoid** chemical, quercetin, on androgen action in an androgen-responsive LNCaP prostate cancer cell line. Western blot anal. showed that AR protein expression was inhibited by quercetin in a dose-dependent manner. To demonstrate that the repression effects on AR expression can actually reduce its function, we found that quercetin inhibited the secretion of the prostate-specific, androgen-regulated tumor markers, PSA and hK2. The mRNA levels of androgen-regulated genes such as PSA, NKX3.1 as well as ornithine decarboxylase (ODC) were down-regulated by quercetin. Transient transfections further showed that quercetin inhibited AR-mediated PSA expression at the transcription level. Finally, it was demonstrated that quercetin could repress the expression of the AR gene at the transcription level. Our result suggests that quercetin can attenuate the function of AR by repressing its expression and has the potential to become a chemopreventive and/or **chemotherapeutic agent** for prostate cancer.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:144762 CAPLUS
DOCUMENT NUMBER: 132:193252
TITLE: Activation and protection of T-cells (CD4+ and CD8+) using an H2 receptor agonist and other T-cell activating agents
INVENTOR(S): Hellstrand, Kristoffer; Hermodsson, Svante; Gehlsen, Kurt R.
PATENT ASSIGNEE(S): Maxim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000010600	A2	20000302	WO 1999-US19211	19990824
WO 2000010600	A3	20000615		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2341742	AA	20000302	CA 1999-2341742	19990824
EP 1107784	A2	20010620	EP 1999-943853	19990824
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002523378	T2	20020730	JP 2000-565920	19990824

TW 576745	B	20040221	TW 1999-88114376		19990922
AU 9956870	A1	20000314	AU 1999-56870		19990924
AU 765625	B2	20030925			
ZA 2001001787	A	20010927	ZA 2001-1787		20010302
US 2003039628	A1	20030227	US 2002-265521		20021003
PRIORITY APPLN. INFO.:			US 1998-139281	A	19980824
			WO 1999-US19211	W	19990824

AB The present invention relates to a method for facilitating activation of T-cells in a patient, comprising: identifying a patient in need of enhanced T-cell activity, administering an effective amount of a T-cell activating composition to the patient, and administering an effective amount of a compound that inhibits the production or release of intercellular reactive oxygen metabolites (ROM) to the patient. The present invention further relates to the use of H2-receptor agonists to augment the effectiveness of vaccines. The vaccine composition may also comprises **chemotherapeutic agent** and/or antiviral agent.

L5 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2000:296079 CAPLUS
DOCUMENT NUMBER:	133:4163
TITLE:	Dietary bioflavonoids induce cleavage in the MLL gene and may contribute to infant leukemia
AUTHOR(S):	Strick, Reiner; Strissel, Pamela L.; Borgers, Susanne; Smith, Steve L.; Rowley, Janet D.
CORPORATE SOURCE:	Department of Medicine, Section of Hematology/Oncology, University of Chicago, Chicago, IL, 60637, USA
SOURCE:	Proceedings of the National Academy of Sciences of the United States of America (2000), 97(9), 4790-4795 CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER:	National Academy of Sciences
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Chromosomal translocations involving the MLL gene occur in .apprx.80% of infant leukemia. The search for possible agents inducing infant leukemia identified bioflavonoids, natural substances in food and dietary supplements, that cause site-specific DNA cleavage in the MLL breakpoint cluster region (BCR) in vivo. The MLL BCR DNA cleavage was shown in primary progenitor hematopoietic cells from healthy newborns and adults and in cell lines; it colocalized with the MLL BCR cleavage site induced by **chemotherapeutic agents**, such as etoposide (VP16) and doxorubicin (Dox). Both in vivo and addnl. in vitro expts. demonstrated topoisomerase II (topo II) as the target of bioflavonoids similar to VP16 and Dox. Based on 20 bioflavonoids tested, we identified a common structure essential for the topo II-induced DNA cleavage. Reversibility expts. demonstrated a religation of the bioflavonoid and the VP16-induced MLL cleavage site. The observations support a 2-stage model of cellular processing of topo II inhibitors. The first and reversible stage of topo II-induced DNA cleavage results in DNA repair, but also rarely in chromosome translocations, whereas the second nonreversible stage leads to cell death because of accumulated DNA damage. Thus, maternal ingestion of bioflavonoids may induce MLL breaks and potentially translocations in utero leading to infant and early childhood leukemia.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2000:759656 CAPLUS
DOCUMENT NUMBER:	134:13161
TITLE:	Polymethoxyflavonoids from Vitex rotundifolia inhibit proliferation by inducing apoptosis in human myeloid leukemia cells
AUTHOR(S):	Ko, W. G.; Kang, T. H.; Lee, S. J.; Kim, N. Y.; Kim,

Y. C.; Sohn, D. H.; Lee, B. H.
CORPORATE SOURCE: College of Pharmacy and Medicinal Resource Research Center, Wonkwang University, Chonbuk, 570-749, S. Korea
SOURCE: Food and Chemical Toxicology (2000), 38(10), 861-865
CODEN: FCTOD7; ISSN: 0278-6915
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Three polymethoxyflavonoids from the fruit of Vitex rotundifolia, namely 2',3',5-trihydroxy-3,6,7-trimethoxyflavone (Vx-1), vitexicarpin (Vx-5) and artemetin (Vx-6), were tested for their antiproliferative activity in human myeloid leukemia HL-60 cells. They showed a dose-dependent decrease in the growth of HL-60 cells. The concns. required for 50% inhibition of the growth (IC50) after 96 h were 4.03 μM, 0.12 μM and 30.98 μM for Vx-1, Vx-5 and Vx-6, resp. Treatment of HL-60 cells with the **flavonoids** induced morphol. changes that are characteristic of apoptosis. We judged the induction of apoptosis by the detection of DNA fragmentation in agarose gel electrophoresis and the degree of apoptosis was quantified by a double-antibody sandwich ELISA and by flow cytometric anal. The C-3 hydroxyl and C-8 methoxyl groups were found not to be essential for the activity, but the C-3' methoxyl instead of hydroxyl group lowered the antiproliferative and apoptosis inducing activity. These results suggest that the polymethoxyflavonoids isolated from V. rotundifolia may be used as potential chemopreventive and **chemotherapeutic agents**.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 19 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:171053 CAPLUS
DOCUMENT NUMBER: 133:53297
TITLE: Application of topoisomerase assays in the evaluation of natural products as antitumor agents
AUTHOR(S): Constantinou, Andreas; Salti, George
CORPORATE SOURCE: Department of Surgical Oncology, University of Illinois, Chicago, IL, USA
SOURCE: Journal of Medicinal Food (1999), 2(3-4), 167-171
CODEN: JMFOFJ; ISSN: 1096-620X
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Initially, DNA topoisomerase (topo) inhibitors found clin. applications as antibiotics and cancer **chemotherapeutic agents**. Recently, we demonstrated that plant flavonoids that inhibit mammalian topo I or topo II might be useful as cancer chemopreventive agents (Constantinou et al., 1995b). Phytochems. can inhibit DNA topoisomerases in different ways; depending on the mode and the type of enzyme, these can be classified as topo I poisons, topo II poisons, topo I antagonists, or topo II antagonists. Correctly classifying topo inhibitors is critical because it provides an important lead as to whether the plant agent can be useful in chemoprevention or in chemotherapy. We outline below a strategy that was designed to identify and classify topo I and II inhibitors.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:258525 CAPLUS
DOCUMENT NUMBER: 129:12382
TITLE: Metabolism of the anticancer drug flavopiridol, a new inhibitor of cyclin dependent kinases, in rat liver
AUTHOR(S): Jager, Walter; Zembsch, Bettina; Wolschann, Peter; Pittenauer, Ernst; Senderowicz, Adrian M.; Sausville,

Edward A.; Sedlacek, Hans H.; Graf, Jurg; Thalhammer, Therese

CORPORATE SOURCE: Institute of Pharmaceutical Chemistry, University of Vienna, Vienna, 1090, Austria

SOURCE: Life Sciences (1998), 62(20), 1861-1873
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Flavopiridol (I) is a promising novel **chemotherapeutic agent** currently undergoing clin. phase I trials. The isolated perfused rat liver system was used to examine hepatic metabolism and biliary disposition of I. Besides I two metabolites were detected by high performance liquid chromatog. in bile and perfusate. Twenty-five min after I (30 μM) addition to the perfusion medium, biliary secretion of metabolite 1 and 2 reached a maximum of 1.04 ± 0.52 and 11.34 ± 4.72 nmol/g.liver.min, resp. Biliary excretion of parent I, however, continuously increased for 60 min up to 406 ± 134 pmol/g liver.min. In the perfusate, metabolite 1 was below detection limit and release of metabolite 2 was low (2.8 ± 0.7 pmol/g liver.min after 60 min). Enzymic hydrolysis with β-glucuronidase, mass spectroscopy and electron absorption spectroscopy revealed that both metabolites are monoglucuronides with the glucuronide in position 5 and 7 of the **flavonoid** core, resp. The amount of I, metabolite 1 and metabolite 2 excreted into bile during the 60 min of perfusion was 1.94 ± 0.91, 5.15 ± 1.95 and 57.29 ± 23.60 % of I cleared from the perfusate during 60 min, resp. In contrast to the structurally similar **flavonoids** genistein and daidzein, no inhibition of UDP-glucuronyltransferase with methylumbelliferone as a substrate was observed indicating that different UDP-glucuronyltransferase isoforms are involved in I metabolism Thus, that glucuronidation is the major mechanism of hepatic I biotransformation. Metabolites are mainly excreted into bile but also released into systemic circulation. The pharmacol. and toxicol. effects of these metabolites remain to be elucidated.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 21 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:489673 CAPLUS

TITLE: Fractionation of plants to discover substances to combat cancer.

AUTHOR(S): Kinghorn, A. D.

CORPORATE SOURCE: College Pharmacy, University Illinois, Chicago, IL, 60612, USA

SOURCE: Book of Abstracts, 214th ACS National Meeting, Las Vegas, NV, September 7-11 (1997), AGRO-126. American Chemical Society: Washington, D. C.
CODEN: 64RNAO
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB Currently there are four classes of plant-derived drugs used as cancer chemotherapeutic agents in the United States, and a number of plant secondary metabolites found in the human diet are of interest as potential cancer **chemotherapeutic agents**. In two sep. colaborative multidisciplinary projects, exts. from predominantly tropical plants have been evaluated for their potential anticancer activity and cancer chemopreventive activity using sep. batteries of cell- and mechanism-based in vitro assays. Activity-guided chromatog. fractionation in the presenter's laboratory in these two cancer-based projects has lead to a wide variety of structurally novel bioactive compds., inclusive of alkaloids, diterpenoids, **flavonoids**, lignans, stilbenoids, triterpenoids, and withanolides, among others. Details of the approaches taken, and of the bioactive compds. obtained, will be discussed.

L5 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:285508 CAPLUS
DOCUMENT NUMBER: 126:314740
TITLE: Phytochemicals: a glimpse into their structural and biological variation
AUTHOR(S): Mbwambo, Zakaria H.; Luyengi, Lumonadio; Kinghorn, A. Douglas
CORPORATE SOURCE: Department of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, Program for Collaborative Research in the Pharmaceutical Sciences, University of Illinois at Chicago, Chicago, IL, 60612, USA
SOURCE: International Journal of Pharmacognosy (1996), 34(5), 335-343
CODEN: IJPYEW; ISSN: 0925-1618
PUBLISHER: Swets & Zeitlinger
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 48 refs. Higher plants have afforded a plethora of structurally varied biol. active secondary metabolite organic mols. and accordingly have been subjected to wide exptl. scrutiny in countries all over the world. Here, the promise of just one phytochem. group, the **flavonoids**, is focused upon. Compds. of this type which have potential use as cancer chemopreventives, cancer **chemotherapeutic agents**, and sucrose substitutes are described.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 23 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:872809 CAPLUS
DOCUMENT NUMBER: 123:329296
TITLE: Quercetin not only inhibits P-glycoprotein efflux activity but also inhibits CYP3A isoenzymes. Reply to letter to the editors.
AUTHOR(S): Scambia, G.; Ranelletti, F. O.; Benedetti-Panici, P.; Vincenzo, R. De; Bonanno, G.; Ferrandina, G.; Piantelli, M.; Mancuso, S.
CORPORATE SOURCE: Facolta di Medicina e Chirurgia "Agostino Gemelli", Universita Cattolica del Sacro Cuore, Rome, I-00168, Italy
SOURCE: Cancer Chemotherapy and Pharmacology (1995), 36(5), 449-50
CODEN: CCPHDZ; ISSN: 0344-5704
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A reply to the letter of M.A. Sarkar (ibid., 448-9, 1995) regarding the possible interaction of quercetin with cytotoxic agents via inhibition of cytochrome P 450 CYP3A. It is granted that therapeutic use of quercetin, particularly in combination with **chemotherapeutic agents**, should be considered with caution. However, it would be important to evaluate the possibility of reducing the therapeutic doses of cytotoxic agents in combination with quercetin, given that this **flavonoid** may increase their bioavailability. The detoxifying activity of quercetin may even prove able to reduce the cytotoxic side effects of **chemotherapeutic agents**.

L5 ANSWER 24 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:155161 CAPLUS
DOCUMENT NUMBER: 124:249399
TITLE: Natural products with immunomodulating and antineoplastic activity
AUTHOR(S): Franz, G.
CORPORATE SOURCE: Inst. Pharmacy, Univ. Regensburg, Regensburg, 93040, Germany

SOURCE: Pharmaceutical and Pharmacological Letters (1995), 5(4), 154-8
CODEN: PPLEE3; ISSN: 0939-9488
PUBLISHER: Medpharm Scientific Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 30 refs. Immunostimulants are compds. leading predominantly to a non specific stimulation of the immunol. defense system. This mode of treatment is an attractive alternative to conventional chemotherapy and prophylaxis of infections especially when the hosts defense mechanisms have to be activated under conditions of impaired immune responsiveness. Today different screening methods for the detection of immunostimulating compds. are available which allow a determination of the functional state and the efficacy of the mononuclear phagocyte system, in vivo and in vitro. These include those that use granulocytes, macrophages, T-lymphocyte populations, lymphocyte mitogenic activity, natural killer cells and complement components as target cells or systems. The list of immunol. active agents currently being investigated is quite extensive and constantly enlarging. Many natural compds. have been tested for this purpose and some have been found to be quite active. Emphasis will be presented upon immunol. active carbohydrates, and **flavonoids**. Mainly for a series of well defined polysaccharides, immune potentiating activities are well documented and closely related to distinct structural features. These biopolymers can be utilized for adjuvant treatment of cancer patients in cotherapy with otherwise immunosuppressive **chemotherapeutic agents**. However, even if the effects are obvious and reproducible in different in vitro and in vivo systems, only very little is known concerning the absorption, distribution and pharmacokinetics of these substances.

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1617SXK

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS	4	OCT 28	KOREAPAT now available on STN
NEWS	5	NOV 30	PHAR reloaded with additional data
NEWS	6	DEC 01	LISA now available on STN
NEWS	7	DEC 09	12 databases to be removed from STN on December 31, 2004
NEWS	8	DEC 15	MEDLINE update schedule for December 2004
NEWS	9	DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	10	DEC 17	COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	11	DEC 17	SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	12	DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13	DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS	14	DEC 30	EPFULL: New patent full text database to be available on STN
NEWS	15	DEC 30	CAPLUS - PATENT COVERAGE EXPANDED
NEWS	16	JAN 03	No connect-hour charges in EPFULL during January and February 2005
NEWS	17	FEB 25	CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS	18	FEB 10	STN Patent Forums to be held in March 2005
NEWS	19	FEB 16	STN User Update to be held in conjunction with the 229th ACS National Meeting on March 13, 2005
NEWS	20	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	21	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	22	FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	23	MAR 02	GBFULL: New full-text patent database on STN
NEWS	24	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	25	MAR 03	MEDLINE file segment of TOXCENTER reloaded

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer

agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:49:39 ON 21 MAR 2005

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'CAPLUS' ENTERED AT 15:49:46 ON 21 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 21 Mar 2005 VOL 142 ISS 13
FILE LAST UPDATED: 20 Mar 2005 (20050320/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s gemcitabine
2344 GEMCITABINE
1 GEMCITABINES
L1 2344 GEMCITABINE
(GEMCITABINE OR GEMCITABINES)

=> s flavonoid?
L2 30430 FLAVONOID?

=> s L1 and L2
L3 4 L1 AND L2

=> d 1-4 L3

L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:41226 CAPLUS
DN 140:105321
TI Methods and compositions relating to isoleucine boroproline compounds
IN Adams, Sharlene; Miller, Glenn T.; Jesson, Michael I.; Jones, Barry
PA Point Therapeutics, Inc., USA
SO PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004004658	A2	20040115	WO 2003-US21405	20030709

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004077601 A1 20040422 US 2003-616694 20030709

PRAI US 2002-394856P P 20020709

US 2002-414978P P 20021001

US 2003-466435P P 20030428

OS MARPAT 140:105321

L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:526480 CAPLUS

DN 138:117325

TI High-throughput measurement of the Tp53 response to anticancer drugs and random compounds using a stably integrated

AU Sohn, Taylor A.; Bansal, Ravi; Su, Gloria H.; Murphy, Kathleen M.; Kern, Scott E.

CS Department of Surgery, The Johns Hopkins Medical Institutions, Baltimore, MD, USA

SO Carcinogenesis (2002), 23(6), 949-957
CODEN: CRNGDP; ISSN: 0143-3334

PB Oxford University Press

DT Journal

LA English

RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:132660 CAPLUS

DN 135:131573

TI Development of cyclin-dependent kinase modulators as novel therapeutic approaches for hematological malignancies

AU Senderowicz, A. M.

CS Molecular Therapeutics Unit, Oral and Pharyngeal Cancer Branch, National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, MD, 20892-4340, USA

SO Leukemia (2001), 15(1), 1-9
CODEN: LEUKED; ISSN: 0887-6924

PB Nature Publishing Group

DT Journal; General Review

LA English

RE.CNT 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:510910 CAPLUS

DN 125:185131

TI Drug resistance against **gemcitabine** and topotecan mediated by constitutive hsp70 overexpression in vitro: Implication of quercetin as sensitizer in chemotherapy

AU Sliutz, G.; Karlseder, J.; Tempfer, C.; Orel, L.; Holzer, G.; Simon, MM

CS Medical School, University Vienna, Vienna, 1090, Austria

SO British Journal of Cancer (1996), 74(2), 172-177
CODEN: BJCAAI; ISSN: 0007-0920

PB Stockton

DT Journal

LA English

```
=> FIL STNGUIDE
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         9.08       9.29

FILE 'STNGUIDE' ENTERED AT 15:51:02 ON 21 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Mar 18, 2005 (20050318/UP).

=> d hist

     (FILE 'HOME' ENTERED AT 15:49:39 ON 21 MAR 2005)

     FILE 'CAPLUS' ENTERED AT 15:49:46 ON 21 MAR 2005
L1          2344 S GEMCITABINE
L2         30430 S FLAVONOID?
L3             4 S L1 AND L2

     FILE 'STNGUIDE' ENTERED AT 15:51:02 ON 21 MAR 2005

=> s circiliol
               0 CIRCILIOL
L4             0 CIRCILIOL

=> s ?flavone?
LEFT TRUNCATION IGNORED FOR '?FLAVONE?' FOR FILE 'STNGUIDE'
L5             0 FLAVONE?
Left truncation is not valid in the specified search field in the
specified file.  The term has been searched without left truncation.
Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID'
would be searched as 'FLAVONOID.'

If you are searching in a field that uses implied proximity, and you
used a truncation symbol after a punctuation mark, the system may
interpret the truncation symbol as being at the beginning of a term.
Implied proximity is used in search fields indexed as single words,
for example, the Basic Index.

=> s ?flavone
LEFT TRUNCATION IGNORED FOR '?FLAVONE' FOR FILE 'STNGUIDE'
L6             0 FLAVONE
Left truncation is not valid in the specified search field in the
specified file.  The term has been searched without left truncation.
Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID'
would be searched as 'FLAVONOID.'

If you are searching in a field that uses implied proximity, and you
used a truncation symbol after a punctuation mark, the system may
interpret the truncation symbol as being at the beginning of a term.
Implied proximity is used in search fields indexed as single words,
for example, the Basic Index.

=> s flavone?
L7             0 FLAVONE?

=> fiel caplus
FIEL IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).
```

```
=> fiel caplus
FIEL IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.78      10.07

FILE 'CAPLUS' ENTERED AT 15:58:45 ON 21 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 21 Mar 2005  VOL 142 ISS 13
FILE LAST UPDATED: 20 Mar 2005  (20050320/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s flavone
         10179 FLAVONE
          9033 FLAVONES
L8       15562 FLAVONE
                (FLAVONE OR FLAVONES)

=> s ?flavone?
L9       26189 ?FLAVONE?

=> s gemcitabine
          2344 GEMCITABINE
             1 GEMCITABINES
L10       2344 GEMCITABINE
                (GEMCITABINE OR GEMCITABINES)

=> s L9 and L10
L11          7 L9 AND L10

=> d 1-7 L11

L11  ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2004:759839  CAPLUS
DN   141:254551
TI   Methods and compositions to determine the chemosensitizing dose of suramin
     used in combination therapy
IN   Au, Jessie L. S.; Wientjes, M. Guillaume
PA   USA
SO   U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of Appl. No. PCT/US02/30210.
     CODEN: USXXCO
DT   Patent
LA   English
```

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004180955	A1	20040916	US 2004-807620	20040324
	WO 2003026574	A2	20030403	WO 2002-US30210	20020924
	WO 2003026574	A3	20040415		

W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CH, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, GH, GM, HP, HU, ID, IL, IN, IS, JP, KE, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MA, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, RO, SD, SG, SI, SK, SL, TN, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI	US 2001-324704P	P	20010924		
	WO 2002-US30210	A2	20020924		

L11 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:41226 CAPLUS
DN 140:105321
TI Methods and compositions relating to isoleucine boroproline compounds
IN Adams, Sharlene; Miller, Glenn T.; Jesson, Michael I.; Jones, Barry
PA Point Therapeutics, Inc., USA
SO PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004004658	A2	20040115	WO 2003-US21405	20030709

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	US 2004077601	A1	20040422	US 2003-616694	20030709
PRAI	US 2002-394856P	P	20020709		
	US 2002-414978P	P	20021001		
	US 2003-466435P	P	20030428		

OS MARPAT 140:105321

L11 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:913055 CAPLUS
DN 139:399770
TI Medical goods comprising heparin or chitosan-based hemocompatible coating
IN Horres, Roland; Linssen, Marita Katharina; Hoffmann, Michael; Faust, Volker; Hoffmann, Erika; Di Biase, Donato
PA Hemoteq G.m.b.H., Germany
SO PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003094990	A1	20031120	WO 2003-DE1253	20030415

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE	10221055	A1	20031127	DE 2002-10221055	20020510
DE	10261986	A1	20040318	DE 2002-10261986	20020510
EP	1501565	A1	20050202	EP 2003-729829	20030415

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRAI	US 2002-378676P	P	20020509
	DE 2002-10221055	A	20020510
	WO 2003-DE1253	W	20030415

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:261608 CAPLUS
DN 138:265631
TI Methods and compositions to determine the chemosensitizing dose of suramin used in combination therapy
IN Au, Jessie L.-S.; Wientjes, M. Guillaume
PA USA
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003026574	A2	20030403	WO 2002-US30210	20020924
WO 2003026574	A3	20040415		

W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM,
DZ, EC, EE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KP,
KR, KZ, LC, LK, LR, LS, LT, LV, MA, MG, MK, MN, MW, MX, MZ, NO,
NZ, OM, PH, PL, RO, SD, SG, SI, SK, SL, TN, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1429713	A2	20040623	EP 2002-766346	20020924

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

US 2004180955	A1	20040916	US 2004-807620	20040324
PRAI US 2001-324704P	P	20010924		
WO 2002-US30210	W	20020924		

L11 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:695764 CAPLUS
DN 137:210932
TI Combination therapy for reduction of toxicity of chemotherapeutic agents
IN Prendergast, Patrick T.
PA Ire.
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002069949	A2	20020912	WO 2002-IB632	20020305

WO 2002069949 A3 20030605
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002169140 A1 20021114 US 2002-91855 20020306
PRAI IE 2001-209 A 20010306

L11 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:555299 CAPLUS
DN 137:103875
TI Redox therapy for tumors
IN Hoffman, Arnold
PA Israel
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002056823	A2	20020725	WO 2002-IL51	20020118
WO 2002056823	C1	20031120		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004018987	A1	20040129	US 2003-621326	20030718
PRAI IL 2001-140970	A	20010118		
WO 2002-IL51	A2	20020118		

L11 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:742053 CAPLUS
DN 133:310142
TI Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction
IN Del Soldato, Piero
PA Nicox S.A., Fr.
SO PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000061537	A2	20001019	WO 2000-EP3234	20000411
WO 2000061537	A3	20010927		

W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,

```
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

To display a particular field or fields, enter the display field
codes.  For a list of the display field codes, enter HELP DISPLAYS at
an arrow prompt (=>).  Examples of formats include: TI; TI,AU; BIB,ST;
TI,IND; TI,SO.  You may specify the format fields in any order and the
information will be displayed in the same order as the format
specification.

All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR,
FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC
to view a specified Accession Number.
ENTER DISPLAY FORMAT (BIB):end

=> d hist

     (FILE 'HOME' ENTERED AT 15:49:39 ON 21 MAR 2005)

     FILE 'CAPLUS' ENTERED AT 15:49:46 ON 21 MAR 2005
L1          2344 S GEMCITABINE
L2         30430 S FLAVONOID?
L3             4 S L1 AND L2

     FILE 'STNGUIDE' ENTERED AT 15:51:02 ON 21 MAR 2005
L4             0 S CIRCILIOL
L5             0 S ?FLAVONE?
L6             0 S ?FLAVONE
L7             0 S FLAVONE?

     FILE 'CAPLUS' ENTERED AT 15:58:45 ON 21 MAR 2005
L8         15562 S FLAVONE
L9         26189 S ?FLAVONE?
L10         2344 S GEMCITABINE
L11            7 S L9 AND L10

=> s chemotherapeutic agent or anticancer compound
         17306 CHEMOTHERAPEUTIC
          1698 CHEMOTHERAPEUTICS
         18613 CHEMOTHERAPEUTIC
                 (CHEMOTHERAPEUTIC OR CHEMOTHERAPEUTICS)
        720621 AGENT
       1029855 AGENTS
       1459468 AGENT
                 (AGENT OR AGENTS)
          8561 CHEMOTHERAPEUTIC AGENT
                 (CHEMOTHERAPEUTIC(W)AGENT)
         30356 ANTICANCER
            46 ANTICANCERS
         30376 ANTICANCER
                 (ANTICANCER OR ANTICANCERS)
         93530 COMPOUND
        792106 COMPOUNDS
        873643 COMPOUND
                 (COMPOUND OR COMPOUNDS)
       1045715 COMPD
       1609487 COMPDS
       2281265 COMPD
                 (COMPD OR COMPDS)
       2661773 COMPOUND
                 (COMPOUND OR COMPD)
           374 ANTICANCER COMPOUND
                 (ANTICANCER(W)COMPOUND)
```

```
L12       8929 CHEMOTHERAPEUTIC AGENT OR ANTICANCER COMPOUND

=> s L9 and L12
L13         32 L9 AND L12

=> s chemotherapeutic agent or anticancer?
          1366 CHEMOTHERAPEUTIC
          1699 CHEMOTHERAPEUTICS
         18613 CHEMOTHERAPEUTIC
                 (CHEMOTHERAPEUTIC OR CHEMOTHERAPEUTICS)
        720621 AGENT
       1029855 AGENTS
       1459468 AGENT
                 (AGENT OR AGENTS)
          8561 CHEMOTHERAPEUTIC AGENT
                 (CHEMOTHERAPEUTIC(W)AGENT)
         30542 ANTICANCER?
L14      38310 CHEMOTHERAPEUTIC AGENT OR ANTICANCER?

=> s L9 and L14
L15         226 L9 AND L14

=> s L1 and L15
L16           3 L1 AND L15

=>  d 1-3 ibib abs

L16  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:759839  CAPLUS
DOCUMENT NUMBER:          141:254551
TITLE:                    Methods and compositions to determine the
                          chemosensitizing dose of suramin used in combination
                          therapy
INVENTOR(S):              Au, Jessie L. S.; Wientjes, M. Guillaume
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of Appl.
                          No. PCT/US02/30210.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    ---------------------    --------
     US 2004180955         A1    20040916    US 2004-807620           20040324
     WO 2003026574         A2    20030403    WO 2002-US30210          20020924
     WO 2003026574         A3    20040415
         W:  AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM,
             DZ, EC, EE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KP,
             KR, KZ, LC, LK, LR, LS, LT, LV, MA, MG, MK, MN, MW, MX, MZ, NO,
             NZ, OM, PH, PL, RO, SD, SG, SI, SK, SL, TN, TT, TZ, UA, UG, US,
             UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                       US 2001-324704P     P  20010924
                                             WO 2002-US30210     A2 20020924
AB   A method for determining a therapeutically effective amount of suramin for
     administering to a patient, who is to receive a cytotoxic agent, which
     comprises the steps of determining the circulating suramin concentration in the
     patient; administering suramin, if required, to establish a low
     circulating concentration of suramin in the patient of below about 200 μM; and
     administering the chemotherapeutic agent to the
```

patient when the low circulating concentration of suramin is present in the patient. Conveniently a nomogram can be constructed for use in clin. settings with the suramin.

L16 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:261608 CAPLUS
DOCUMENT NUMBER: 138:265031
TITLE: Methods and compositions to determine the chemosensitizing dose of suramin used in combination therapy
INVENTOR(S): Au, Jessie L.-S.; Wientjes, M. Guillaume
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003026574	A2	20030403	WO 2002-US30210	20020924
WO 2003026574	A3	20040415		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MA, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, RO, SD, SG, SI, SK, SL, TN, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1429713	A2	20040623	EP 2002-766346	20020924
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2004180955	A1	20040916	US 2004-807620	20040324
PRIORITY APPLN. INFO.:			US 2001-324704P P	20010924
			WO 2002-US30210 W	20020924

AB A method for determining a therapeutically effective amount of suramin for administering to a patient who is to receive a cytotoxic agent comprises determining the circulating suramin concentration in the patient; administering suramin, if required, to establish a low circulating concentration of suramin in the patient of below about 200 μM; and administering the chemotherapeutic agent to the patient when the low circulating concentration of suramin is present in the patient. Conveniently a nomogram can be constructed for use in clin. settings with the suramin.

L16 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:695764 CAPLUS
DOCUMENT NUMBER: 137:210932
TITLE: Combination therapy for reduction of toxicity of **chemotherapeutic agents**
INVENTOR(S): Prendergast, Patrick T.
PATENT ASSIGNEE(S): Ire.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002069949	A2	20020912	WO 2002-IB632	20020305

```
     WO 2002069949         A3    20030605
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
             GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
             GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2002169140         A1    20021114    US 2002-91855          20020306
PRIORITY APPLN. INFO.:                       IE 2001-209         A  20010306
AB   Provided in the present invention are compds. suitable for treating
     neoplasms and tumors, viral, bacterial and parasite infections and
     combination therapy with these agents to lower the adverse side effects.


=> d hist

     (FILE 'HOME' ENTERED AT 15:49:39 ON 21 MAR 2005)

     FILE 'CAPLUS' ENTERED AT 15:49:46 ON 21 MAR 2005
L1          2344 S GEMCITABINE
L2         30430 S FLAVONOID?
L3             4 S L1 AND L2

     FILE 'STNGUIDE' ENTERED AT 15:51:02 ON 21 MAR 2005
L4             0 S CIRCILIOL
L5             0 S ?FLAVONE?
L6             0 S ?FLAVONE
L7             0 S FLAVONE?

     FILE 'CAPLUS' ENTERED AT 15:58:45 ON 21 MAR 2005
L8         15562 S FLAVONE
L9         26189 S ?FLAVONE?
L10         2344 S GEMCITABINE
L11            7 S L9 AND L10
L12         8929 S CHEMOTHERAPEUTIC AGENT OR ANTICANCER COMPOUND
L13           32 S L9 AND L12
L14        38310 S CHEMOTHERAPEUTIC AGENT OR ANTICANCER?
L15          226 S L9 AND L14
L16            3 S L1 AND L15

=> s circiliol or cirsiciol
               1 CIRCILIOL
               0 CIRSICIOL
L17            1 CIRCILIOL OR CIRSICIOL

=> d l17

L17  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   1994:431157  CAPLUS
DN   121:31157
TI   Steroidal compounds from Teucrium chamaedrys subsp. chamaedrys
AU   Ulubelen, A.; Topcu, G.; Kaya, U.
CS   Fac. Pharm., Univ. Istanbul, Istanbul, 34452, Turk.
SO   Phytochemistry (1994), 36(1), 171-3
     CODEN: PYTCAS; ISSN: 0031-9422
DT   Journal
LA   English


=> s circiliol or cirsiliol
               1 CIRCILIOL
```

```
L13          32 S L9 AND L12
L14       38310 S CHEMOTHERAPEUTIC AGENT OR ANTICANCER?
L15         226 S L9 AND L14
L16           3 S L1 AND L15
L17           1 S CIRCILIOL OR CIRSICIOL
L18         125 S CIRCILIOL OR CIRSILIOL
L19           1 S L18 AND L15
L20           1 S L18 AND L12
L21           1 S L18 AND L10

=> d 1-32 IBIB abs L13

L13  ANSWER 1 OF 32  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:53052  CAPLUS
DOCUMENT NUMBER:          142:190260
TITLE:                    Genistein, a soy isoflavone, enhances
                          necrotic-like cell death in a breast cancer cell
                          treated with a chemotherapeutic
                          agent
AUTHOR(S):                Satoh, Haruna; Nishikawa, Kazuhiro; Suzuki, Kazuyuki;
                          Asano, Ryuji; Virgona, Nantiga; Ichikawa, Tomio;
                          Hagiwara, Kiyokazu; Yano, Tomohiro
CORPORATE SOURCE:         Department of Food Science Research for Health,
                          National Institute of Health and Nutrition, Tokyo,
                          162-8636, Japan
SOURCE:                   Research Communications in Molecular Pathology and
                          Pharmacology (2003), 113-114, 149-158
                          CODEN: RCMPE6; ISSN: 1078-0297
PUBLISHER:                PJD Publications Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Genistein is a major component of soybean isoflavone and has
     preventive effect against breast cancer.  In breast cancer, the
     over-expression of HER-2 contributes to malignant transformation of the
     cancer cells.  The present study was undertaken to estimate if genistein could
     act as a useful anti-cancer agent against a breast cancer cell
     over-expressing HER-2 in combination with a conventional chemotherapy
     agent, adriamycin (ADR).  Genistein enhanced cytotoxic effect of ADR at
     low doses < IC50 against the human breast cancer cell.  The enhancing
     effect was mainly dependent on the elevation of necrotic-like cell death
     but not apoptotic cell death.  In conjugation with this event, remarkable
     inactivation of HER-2 and Akt in the breast cancer cell was caused by the
     combination of genistein and ADR.  These results suggest that genistein
     enhances necrotic-like cell death of the breast cancer cells through the
     inactivation of HER-2 receptor and Akt in combination with ADR.
REFERENCE COUNT:          26    THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13  ANSWER 2 OF 32  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:958643  CAPLUS
DOCUMENT NUMBER:          142:173464
TITLE:                    Anticancer compounds isolated from
                          leaves of Crinum latifolium, derivatives thereof and
                          anticancer composition containing the same
INVENTOR(S):              Ahn, Byung Zun
PATENT ASSIGNEE(S):       S. Korea
SOURCE:                   Repub. Korean Kongkae Taeho Kongbo, No pp. given
                          CODEN: KRXXA7
DOCUMENT TYPE:            Patent
LANGUAGE:                 Korean
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
     ---------------      ----   --------    --------------------   --------
```

KR 2003061981 A 20030723 KR 2002-2145 20020114
PRIORITY APPLN. INFO.: KR 2002-2145 20020114
AB **Anticancer compds.** isolated from leaves of Crinum latifolium, derivs. thereof and an anticancer composition containing the same are provided, thereby preventing and treating cancers effectively. Anticancer compds. isolated from leaves of Crinum latifolium include 6,7-dimethoxy-4-(3-methyl-2-butenoyloxymethyl)coumarin of the formula I, and 5,6,3-trihydroxy-7,8,4-trimethoxyflavon of the formula II. Another **anticancer compound** represented by the formula III is provided, wherein R is C1-C3 alkyl. A process for preparing the compound of the formula III comprises the steps of: (i) condensing 3,4-dioxyphenol and Et 4-chloroacetate by a Pechman method in sulfuric acid to prepare 4-chloromethyl-6,7-dimethoxycoumarin; and (ii) reacting 4-chloromethyl-6,7-dimethoxycoumarin with organic acid in the presence of triethylamine.

L13 ANSWER 3 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:759839 CAPLUS
DOCUMENT NUMBER: 141:254551
TITLE: Methods and compositions to determine the chemosensitizing dose of suramin used in combination therapy
INVENTOR(S): Au, Jessie L. S.; Wientjes, M. Guillaume
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of Appl. No. PCT/US02/30210.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004180955	A1	20040916	US 2004-807620	20040324
WO 2003026574	A2	20030403	WO 2002-US30210	20020924
WO 2003026574	A3	20040415		

W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MA, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, RO, SD, SG, SI, SK, SL, TN, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-324704P P 20010924
WO 2002-US30210 A2 20020924
AB A method for determining a therapeutically effective amount of suramin for administering to a patient, who is to receive a cytotoxic agent, which comprises the steps of determining the circulating suramin concentration in the patient; administering suramin, if required, to establish a low circulating concentration of suramin in the patient of below about 200 μM; and administering the **chemotherapeutic agent** to the patient when the low circulating concentration of suramin is present in the patient. Conveniently a nomogram can be constructed for use in clin. settings with the suramin.

L13 ANSWER 4 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:675947 CAPLUS
DOCUMENT NUMBER: 141:325120
TITLE: Clinical characteristics and pharmacokinetics of purified soy **isoflavones**: Multiple-dose administration to men with prostate neoplasia

AUTHOR(S): Fischer, Leslie; Mahoney, Chrysa; Jeffcoat, A. Robert; Koch, Matthew A.; Thomas, Brian F.; Valentine, John L.; Stinchcombe, Thomas; Boan, Jarol; Crowell, James A.; Zeisel, Steven H.

CORPORATE SOURCE: Department of Nutrition, School of Public Health, School of Medicine, University of North Carolina, Chapel Hill, NC, 27599-7461, USA

SOURCE: Nutrition and Cancer (2004), 48(2), 160-170
CODEN: NUCADQ; ISSN: 0163-5581

PUBLISHER: Lawrence Erlbaum Associates, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A phase I clin. trial was conducted to determine the safety, pharmacokinetic parameters, and efficacy of orally administered **isoflavones** (genistein and daidzein, potential cancer **chemotherapeutic agents**) over a 3-mo period in men with prostate neoplasia. Twenty men, ages 40 and above, with stage B, C, or D adenocarcinoma of the prostate were treated with a multiple-dose regimen of a soy **isoflavone** formulation (delivering approx. 300 or 600 mg/day genistein and half this much daidzein) for 84 days. The delivered dose of **isoflavones** was more than 10-fold higher than that typically taken by prostate cancer patients. In men with prostate cancer, relatively minor side effects of chronic **isoflavone** treatment were observed including some estrogenic effects (breast changes, increased frequency of hot flashes). Serum dehydroepiandrosterone was decreased by 31.7% (P = 0.0004) at the end of treatment. Except for those subjects whose prostate-specific antigen (PSA) values were below 0.4 ng/mL, subjects had a history of increasing PSA levels prior to the trial. This increase continued during the trial both while on soy **isoflavones** and after treatment was discontinued. On average the rate of rise accelerated after soy **isoflavones** were discontinued, but that difference did not attain statistical significance. Genistein and daidzein were rapidly cleared from plasma and excreted in urine. Pharmacokinetic data for chronic dose administration were similar to single-dose administration for the **isoflavones** investigated except that we observed slightly longer circulation time for daidzein.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:384103 CAPLUS

DOCUMENT NUMBER: 141:17096

TITLE: Genistein inversely affects tubulin-binding agent-induced apoptosis in human breast cancer cells

AUTHOR(S): Liao, Cho-Hwa; Pan, Shiow-Lin; Guh, Jih-Hwa; Teng, Che-Ming

CORPORATE SOURCE: College of Medicine, Pharmacological Institute, National Taiwan University, Taipei, 100, Taiwan

SOURCE: Biochemical Pharmacology (2004), 67(11), 2031-2038
CODEN: BCPCA6; ISSN: 0006-2952

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Genistein, a natural **isoflavone** phytoestrogen present in soybeans, has been extensively studied as a chemopreventive or therapeutic agent in several types of cancer. The traditional Asian diet is rich in soy products may explain in part why the incidence of breast cancer in Asian women is relatively low. To improve therapeutic benefits, we investigated the combination of genistein with **chemotherapeutic agents** in phenotypically dissimilar human breast cancer cells, MCF-7 and MDA-MB-231, in which estrogen receptor expression is pos. and neg., resp. In the present study, genistein significantly decreased cell apoptosis induced by tubulin-binding agents, paclitaxel and vincristine. FACScan anal. revealed that genistein also diminished the accumulation of the G2/M phase in the cell cycle caused by tubulin-binding agents. In

situ staining of microtubules revealed that genistein could decrease paclitaxel-induced tubulin polymerization However, in vivo tubulin polymerization assay revealed that simultaneous treatment of genistein did not change the tubulin/microtubule dynamic. Genistein reduced Bcl-2 phosphorylation triggered by paclitaxel and vincristine without changing Bax protein expression. p53 and p21 expression, monitored by Western blotting, was not altered by genistein. However, the expression of cyclin B1 and CDC2 kinase was markedly decreased in combination with genistein. In conclusion, genistein inversely affected tubulin-binding agent-induced apoptosis via down-regulation of cyclin B1/CDC2 kinase expression resulting in reduced Bcl-2 phosphorylation.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:310964 CAPLUS
DOCUMENT NUMBER: 140:297495
TITLE: Synergistic anticancer compositions containing platinum-isoflavonoids
INVENTOR(S): Kelly, Graham Edmund
PATENT ASSIGNEE(S): Novogen Research Pty. Ltd., Australia
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004030662	A1	20040415	WO 2003-AU1296	20031002

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: AU 2002-951833 A 20021002
OTHER SOURCE(S): MARPAT 140:297495
AB This invention relates to combination therapies involving anticancer **chemotherapeutic agents** and **isoflavones** or analogs thereof. The invention further relates to compds., compns., methods and therapeutic uses involving, containing, comprising, including and/or for preparing platinum-isoflavonoid complexes suitable for use in the combination therapies of the invention. The effect of a composition comprising cisplatin and dehydroequol on various cancer cell lines in culture plates was assessed. It was found that the amount of cisplatin needed to kill a set number of cancer cells was less when in admixt. with dehydroequol as compared to controls with cisplatin alone. Dehydroequol was found to exhibit a strong synergistic interaction with cisplatin in cell lines derived from ovarian, prostate and pancreatic cancers.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:965772 CAPLUS
DOCUMENT NUMBER: 140:385592
TITLE: Cytostatic and cytotoxic activity of synthetic genistein glycosides against human cancer cell lines
AUTHOR(S): Polkowski, Krzysztof; Popiolkiewicz, Joanna;

Krzeczynski, Piotr; Ramza, Jan; Pucko, Wieslaw; Zegrocka-Stendel, Oliwia; Boryski, Jerzy; Skierski, Janusz S.; Mazurek, Aleksander P.; Grynkiewicz, Grzegorz

CORPORATE SOURCE: National Institute of Public Health, Warsaw, 00-725, Pol.

SOURCE: Cancer Letters (Amsterdam, Netherlands) (2004), 203(1), 59-69
CODEN: CALEDQ; ISSN: 0304-3835

PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Genistein, the principal soy **isoflavone**, is a mol. of great interest as an innovative **chemotherapeutic agent** or as a lead-compound in anticancer drug design. To enhance intrinsic activity of genistein and to explore its pharmacophoric potential, its glycosidic derivs. were synthesized. On the basis of structural features and calculated lipophilicity coefficient (C log P) the derivs. were classified as hydrophilic (i.e. those containing free sugar moiety) or lipophilic (i.e. those with alkylated or acylated sugar hydroxyls). The in vitro cytostatic and cytotoxic studies showed hydrophilic glycosides to be practically inactive against human cancer cell lines when compared to the free aglycon. On the contrary, lipophilic glycosides were significantly more active than the parent **isoflavone** although the correlation between C log P and the activity was not clear. On the basis of GI50 and LC50 values two of the most active glycosides were found to be several times more potent in their cytostatic and cytotoxic effect than genistein. Addnl. all lipophilic glycosides were revealed to exhibit different mode of action in comparison to genistein. It may suggest that these compds. do not undergo rapid biodegrdn., either in culture media or inside cells, and exert their biol. effects primarily as intact mols.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:376630 CAPLUS
DOCUMENT NUMBER: 138:374200
TITLE: Chemoprotectant compositions containing **isoflavones**
INVENTOR(S): Shapiro, Alla
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003039537	A1	20030515	WO 2002-US35437	20021105

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-330976P P 20011105
OTHER SOURCE(S): MARPAT 138:374200

AB A non-toxic and effective **isoflavone** chemoprotectant agent for

treating or preventing effects and damage due to the administration of **chemotherapeutic agents** in the treatment of cancer and other conditions and diseases is described. The **isoflavone** can be administered orally, s.c., i.m., i.v., transdermally, intranasally, or rectally. The **isoflavone** is administered chronically, and/or before, during and/or after administration of the **chemotherapeutic agent**. For example, in patients with breast cancer undergoing treatment with chemotherapeutic agents that cause severe cardiac toxicity, administration of genistein (0.1-1000 mg/kg) prior and during chemotherapy resulted in decreased cardiotoxicity, allowing an increase in drug intensity, shortened delay in drug administration between doses of the **chemotherapeutic agent**, and reduced side effects.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 9 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:261608 CAPLUS
DOCUMENT NUMBER: 138:265631
TITLE: Methods and compositions to determine the chemosensitizing dose of suramin used in combination therapy
INVENTOR(S): Au, Jessie L.-S.; Wientjes, M. Guillaume
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003026574	A2	20030403	WO 2002-US30210	20020924
WO 2003026574	A3	20040415		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MA, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, RO, SD, SG, SI, SK, SL, TN, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1429713	A2	20040623	EP 2002-766346	20020924
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2004180955	A1	20040916	US 2004-807620	20040324
PRIORITY APPLN. INFO.:			US 2001-324704P P	20010924
			WO 2002-US30210 W	20020924

AB A method for determining a therapeutically effective amount of suramin for administering to a patient who is to receive a cytotoxic agent comprises determining the circulating suramin concentration in the patient; administering suramin, if required, to establish a low circulating concentration of suramin in the patient of below about 200 μM; and administering the **chemotherapeutic agent** to the patient when the low circulating concentration of suramin is present in the patient. Conveniently a nomogram can be constructed for use in clin. settings with the suramin.

L13 ANSWER 10 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:695764 CAPLUS
DOCUMENT NUMBER: 137:210932
TITLE: Combination therapy for reduction of toxicity of **chemotherapeutic agents**

INVENTOR(S): Prendergast, Patrick T.
PATENT ASSIGNEE(S): Ire.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002069949	A2	20020912	WO 2002-IB632	20020305
WO 2002069949	A3	20030605		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002169140	A1	20021114	US 2002-91855	20020306
PRIORITY APPLN. INFO.:			IE 2001-209 A	20010306

AB Provided in the present invention are compds. suitable for treating neoplasms and tumors, viral, bacterial and parasite infections and combination therapy with these agents to lower the adverse side effects.

L13 ANSWER 11 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:512399 CAPLUS
DOCUMENT NUMBER: 138:214709
TITLE: 5,6-Dimethylxanthenone-4-Acetic Acid (DMXAA): a New Biological Response Modifier for Cancer Therapy
AUTHOR(S): Zhou, Shufeng; Kestell, Philip; Baguley, Bruce C.; Paxton, James W.
CORPORATE SOURCE: Division of Pharmacology and Clinical Pharmacology, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, N. Z.
SOURCE: Investigational New Drugs (2002), 20(3), 281-295
CODEN: INNDDK; ISSN: 0167-6997
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The investigational anti-cancer drug 5,6-dimethylxanthenone-4-acetic acid (DMXAA) was developed by the Auckland Cancer Society Research Center (ACSRC). It has recently completed Phase I trials in New Zealand and UK under the direction of the Cancer Research Campaign's Phase I/II Clin. Trials Committee. As a biol. response modifier, pharmacol. and toxicol. properties of DMXAA are remarkably different from most conventional **chemotherapeutic agents.** Induction of cytokines (particularly tumor necrosis factor (TNF-α), serotonin and nitric oxide (NO)), anti-vascular and anti-angiogenic effects are considered to be major mechanisms of action based on in vitro and animal studies. In cancer patients of Phase I study, DMXAA also exhibited various biol. effects, including induction of TNF-α, serotonin and NO, which are consistent with those effects observed in in vitro and animal studies. Preclin. studies indicated that DMXAA had more potent anti-tumor activity compared to **flavone**-8-acetic acid (FAA). In contrast to FAA that did not show anti-tumor activity in cancer patients, DMXAA (22 mg/kg by i.v. infusion over 20 min) resulted in partial response in one patient with metastatic cervical squamous carcinoma in a Phase I study where 65 cancer patients were enrolled in New Zealand. The maximum tolerated dose (MTD) in mouse, rabbit, rat and human was 30, 99, 330, and 99 mg/kg resp. The dose-limiting toxicity of DMXAA in cancer patients included

acute reversible tremor, cognitive impairment, visual disturbance, dyspnoea and anxiety. The plasma protein binding and distribution into blood cells of DMXAA are dependent on species and drug concentration DMXAA is extensively metabolized, mainly by glucuronidation of its acetic acid side chain and 6-methylhydroxylation, giving rise to DMXAA acyl glucuronide (DMXAA-G), and 6-hydroxymethyl-5-methylxanthenone-4-acetic acid (6 OH-MAA), which are excreted into bile and urine. DMXAA-G has been shown to be chemical reactive, undergoing hydrolysis, intramol. migration and covalent binding. Studies have indicated that DMXAA glucuronidation is catalyzed by uridine diphosphate glucuronosyltransferases (UGT1A9 and UGT2B7), and 6-methylhydroxylation by cytochrome P 450 (CYP1A2). Non-linear plasma pharmacokinetics of DMXAA has been observed in animals and patients, presumably due to saturation of the elimination process and plasma protein binding. Species differences in DMXAA plasma pharmacokinetics have been observed, with the rabbit having the greatest plasma clearance, followed by the human, rat and mouse. In vivo disposition studies in these species did not provide an explanation for the differences in MTD. Co-administration of DMXAA with other drugs has been shown to result in enhanced anti-tumor activity and alterations in pharmacokinetics, as reported for the combination of DMXAA with melphalan, thalidomide, cyproheptadine, and the bioreductive agent tirapazamine, in mouse models. Species-dependent DMXAA-thalidomide pharmacokinetic interactions have been observed Co-administration of thalidomide significantly increased the plasma area of the plasma concentration-time curve (AUC) of DMXAA in mice, but had no effect on DMXAA's pharmacokinetics in the rat. It appears that the pharmacol. and toxicol. properties of DMXAA as a new biol. response modifier are unlikely to be predicted based on preclin. studies. Similar to many biol. response modifiers, DMXAA alone did not show striking anti-tumor activity in patients. However, preclin. studies of DMXAA-drug combinations indicate that DMXAA may have a potential role in cancer treatment when co-administered with other drugs. Further studies are required to explore the mol. targets of DMXAA and mechanisms for the interactions with other drugs co-administered during combination treatment, which may allow for the optimization of DMXAA-based chemotherapy.

REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 12 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:190263 CAPLUS

TITLE: Synthesis, SAR and biological evaluation of zapotin as a chemoprevention agent

AUTHOR(S): Hirschelman, Wendy H.; Park, Eun Jung; Murillo, Genoveva; Hawthorne, Michael; Kosmeder, Jerome W., II; Mehta, Rajendra; Pezzuto, John M.; Moriarty, Robert M.

CORPORATE SOURCE: Department of Chemistry, College of Liberal Arts and Sciences, University of Illinois at Chicago, Chicago, IL, 60607, USA

SOURCE: Abstracts of Papers, 223rd ACS National Meeting, Orlando, FL, United States, April 7-11, 2002 (2002), MEDI-144. American Chemical Society: Washington, D. C.
CODEN: 69CKQP

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Zapotin (5,6,2',6,-**tetramethoxyflavone**, 13) is a natural product found in the seeds of the edible plant, Casimiroa edulis. This **flavone** was isolated and evaluated in HT-29 and MMOC assays and found to be active as a chemopreventive and **chemotherapeutic agent**. Based on these results, zapotin (13) and other structurally modified analogs 1-12, 14 were synthesized. The synthetic samples were tested in HL-60 (leukemia cell line), MMOC (mouse mammary organ culture), HT-29 (colon cancer carcinoma cell line) and QR (quinone reductase) screening assays. A structure-activity (SAR) model was established and three potent chemoprevention agents were discovered.

L13 ANSWER 13 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:833064 CAPLUS
DOCUMENT NUMBER: 135:352781
TITLE: Compositions and methods for protecting cells during cancer chemotherapy and radiotherapy
INVENTOR(S): Fuhl, William E.; Raghavachari, Nalini; Zhu, Ming; Kink, John
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001085142	A1	20011115	WO 2001-US14464		20010504
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2408152	AA	20011115	CA 2001-2408152		20010504
EP 1280556	A1	20030205	EP 2001-933017		20010504
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004515453	T2	20040527	JP 2001-581796		20010504
US 2005043224	A1	20050224	US 2004-881028		20040630
PRIORITY APPLN. INFO.:			US 2000-565714	A	20000505
			WO 2001-US14464	W	20010504

AB Compns., pharmaceutical prepns. and methods are disclosed for protecting non-neoplastic cells from damage caused by cancer chemotherapeutic agents or radiation therapy, during the course of cancer therapy or bone marrow transplant. These are based on the use of chemoprotective inducing agents that induce or increase production of cellular detoxification enzymes in target cell populations. The compns. and methods are useful to reduce or prevent hair loss, gastrointestinal distress and lesions of the skin and oral mucosa that commonly occur in patients undergoing cancer therapy. Also disclosed is a novel assay system for identifying new chemoprotective inducing agents.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 14 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:759656 CAPLUS
DOCUMENT NUMBER: 134:13161
TITLE: Polymethoxyflavonoids from Vitex rotundifolia inhibit proliferation by inducing apoptosis in human myeloid leukemia cells
AUTHOR(S): Ko, W. G.; Kang, T. H.; Lee, S. J.; Kim, N. Y.; Kim, Y. C.; Sohn, D. H.; Lee, B. H.
CORPORATE SOURCE: College of Pharmacy and Medicinal Resource Research Center, Wonkwang University, Chonbuk, 570-749, S. Korea
SOURCE: Food and Chemical Toxicology (2000), 38(10), 861-865
CODEN: FCTOD7; ISSN: 0278-6915
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three polymethoxyflavonoids from the fruit of Vitex rotundifolia, namely 2',3',5-trihydroxy-3,6,7-**trimethoxyflavone** (Vx-1), vitexicarpin (Vx-5) and artemetin (Vx-6), were tested for their antiproliferative activity in human myeloid leukemia HL-60 cells. They showed a dose-dependent decrease in the growth of HL-60 cells. The concns. required for 50% inhibition of the growth (IC50) after 96 h were 4.03 μM, 6.12 μM and 30.56 μM for Vx-1, Vx-5 and Vx-6, resp. Treatment of HL-60 cells with the flavonoids induced morphol. changes that are characteristic of apoptosis. We judged the induction of apoptosis by the detection of DNA fragmentation in agarose gel electrophoresis and the degree of apoptosis was quantified by a double-antibody sandwich ELISA and by flow cytometric anal. The C-3 hydroxyl and C-8 methoxyl groups were found not to be essential for the activity, but the C-3' methoxyl instead of hydroxyl group lowered the antiproliferative and apoptosis inducing activity. These results suggest that the polymethoxyflavonoids isolated from V. rotundifolia may be used as potential chemopreventive and **chemotherapeutic agents.**

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 15 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:646580 CAPLUS
DOCUMENT NUMBER: 133:317103
TITLE: The therapeutic potential of flavonoids
AUTHOR(S): Wang, Hui-Kang
CORPORATE SOURCE: University of North Carolina, Chapel Hill, NC, USA
SOURCE: Expert Opinion on Investigational Drugs (2000), 9(9), 2103-2119
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 92 refs. Four most widely investigated flavonoids, flavopiridol, catechins, genistein and quercetin are reviewed in this article. Flavopiridol is a novel semisynthetic **flavone** analog of rohitukine, a leading **anticancer compound** from an Indian tree. Flavopiridol inhibits most cyclin-dependent kinases and displays unique anticancer properties. It is the first cyclin-dependent kinase inhibitor to be tested in Phase II clin. trials. Catechin and its gallate are major ingredients in green tea and their anti-oxidant and cancer preventive effects have been widely investigated. A Phase I study of green tea extract GTE-TP91 has been conducted in adult patients with solid tumors. Similarly, genistein is a major ingredient in soybean and has been shown to prevent cancer and have antitumor, anti-oxidant and anti-inflammatory effects. Two antibody-genistein conjugates, B43-genistein and EGF-genistein, are currently in clin. development for the treatment of acute lymphoblastic leukemia and breast cancer, resp. Finally, most recent updates of quercetin are briefly described.

REFERENCE COUNT: 92 THERE ARE 92 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 16 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:296079 CAPLUS
DOCUMENT NUMBER: 133:4163
TITLE: Dietary bioflavonoids induce cleavage in the MLL gene and may contribute to infant leukemia
AUTHOR(S): Strick, Reiner; Strissel, Pamela L.; Borgers, Susanne; Smith, Steve L.; Rowley, Janet D.
CORPORATE SOURCE: Department of Medicine, Section of Hematology/Oncology, University of Chicago, Chicago, IL, 60637, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(9), 4790-4795
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Chromosomal translocations involving the MLL gene occur in .apprx.80% of infant leukemia. The search for possible agents inducing infant leukemia identified bioflavonoids, natural substances in food and dietary supplements, that cause site-specific DNA cleavage in the MLL breakpoint cluster region (BCR) in vivo. The MLL BCR DNA cleavage was shown in primary progenitor hematopoietic cells from healthy newborns and adults and in cell lines; it colocalized with the MLL BCR cleavage site induced by **chemotherapeutic agents**, such as etoposide (VP16) and doxorubicin (Dox). Both in vivo and addnl. in vitro expts. demonstrated topoisomerase II (topo II) as the target of bioflavonoids similar to VP16 and Dox. Based on 20 bioflavonoids tested, we identified a common structure essential for the topo II-induced DNA cleavage. Reversibility expts. demonstrated a religation of the bioflavonoid and the VP16-induced MLL cleavage site. The observations support a 2-stage model of cellular processing of topo II inhibitors. The first and reversible stage of topo II-induced DNA cleavage results in DNA repair, but also rarely in chromosome translocations, whereas the second nonreversible stage leads to cell death because of accumulated DNA damage. Thus, maternal ingestion of bioflavonoids may induce MLL breaks and potentially translocations in utero leading to infant and early childhood leukemia.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 17 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:227537 CAPLUS
DOCUMENT NUMBER: 132:262172
TITLE: Use of neoangiogenesis markers for diagnosis and treatment of tumors
INVENTOR(S): Krause, Werner; Muschick, Peter
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018439	A2	20000406	WO 1999-EP7198	19990929
WO 2000018439	A3	20000914		
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, EE, ES, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19845798	A1	20000413	DE 1998-19845798	19980929
PRIORITY APPLN. INFO.:			DE 1998-19845798 A	19980929

AB Neoangiogenesis markers (i.e. antibodies or receptors for e.g. vascular endothelial growth factor, placenta growth factor, acidic or basic FGF, transforming growth factor α or β, hepatocyte growth factor, insulin-like growth factor I, glycoprotein B61, protein LERK-1, flk-1 receptor, etc.) or partial sequences thereof and antiangiogenic compds. and factors such as paclitaxel, endostatin, fibronectin peptide, and fumagillin are conjugated with active agents such as **chemotherapeutic agents**, radiosensitizers, photosensitizers, antibodies, oligonucleotides, radioactive metal complexes, etc., which may be bound to carriers, for treatment of tumors. Likewise, neoangiogenesis markers may be conjugated to diagnostic agents such as MRI, radiog., ultrasound, or near-IR contrast agents for tumor diagnosis. Thus, N',N',N''',N'''-tetrakis(tert-butoxycarboxymethyl)-N''-

(hydroxycarboxymethyl)diethylenetriamine was converted to its N-hydroxysuccinimide ester, coupled to a Thy-1 antibody, complexed with 186Re, and injected i.v. into rabbits for detection of implanted VX2 tumors by scintigraphy with a gamma camera.

L13 ANSWER 18 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:144702 CAPLUS
DOCUMENT NUMBER: 132:193252
TITLE: Activation and protection of T-cells (CD4+ and CD8+) using an H2 receptor agonist and other T-cell activating agents
INVENTOR(S): Hellstrand, Kristoffer; Hermodsson, Svante; Gehlsen, Kurt R.
PATENT ASSIGNEE(S): Maxim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000010600	A2	20000302	WO 1999-US19211		19990824
WO 2000010600	A3	20000615			
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2341742	AA	20000302	CA 1999-2341742		19990824
EP 1107784	A2	20010620	EP 1999-943853		19990824
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002523378	T2	20020730	JP 2000-565920		19990824
TW 576745	B	20040221	TW 1999-88114376		19990922
AU 9956870	A1	20000314	AU 1999-56870		19990924
AU 765625	B2	20030925			
ZA 2001001787	A	20010927	ZA 2001-1787		20010302
US 2003039628	A1	20030227	US 2002-265521		20021003
PRIORITY APPLN. INFO.:			US 1998-139281	A	19980824
			WO 1999-US19211	W	19990824

AB The present invention relates to a method for facilitating activation of T-cells in a patient, comprising: identifying a patient in need of enhanced T-cell activity, administering an effective amount of a T-cell activating composition to the patient, and administering an effective amount of a compound that inhibits the production or release of intercellular reactive oxygen metabolites (ROM) to the patient. The present invention further relates to the use of H2-receptor agonists to augment the effectiveness of vaccines. The vaccine composition may also comprises **chemotherapeutic agent** and/or antiviral agent.

L13 ANSWER 19 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:574904 CAPLUS
DOCUMENT NUMBER: 131:295069
TITLE: Oxidative metabolism of monensin in rat liver microsomes and interactions with tiamulin and other **chemotherapeutic agents**: evidence for the involvement of cytochrome P-450 3A subfamily
AUTHOR(S): Nebbia, Carlo; Ceppa, Luciano; Dacasto, Mauro;

Carletti, Monica; Nachtmann, Carlo
CORPORATE SOURCE: Department of Animal Pathology, Division of Pharmacology and Toxicology, University of Turin, Turin, 10126, Italy
SOURCE: Drug Metabolism and Disposition (1999), 27(9), 1039-1044
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Monensin (MON) is an ionophore antibiotic widely used in veterinary practice as a coccidiostatic or a growth promoter. The aims of this study were to characterize the P 450 isoenzyme(s) involved in the biotransformation of the ionophore and to investigate how this process may be affected by tiamulin and other **chemotherapeutic agents** known to produce toxic interactions with MON when administered concurrently in vivo. In liver microsomes from untreated rats (UT) or from rats pretreated, resp., with ethanol (ETOH), β-**naphthoflavone** (βNAF), phenobarbital (PB), pregnenolone 16α-carbonitrile (PCN), or dexamethasone (DEX), the rate of MON O-demethylation was the following: DEX > PCN > PB » UT = ETOH > βNAF; similar results were obtained by measuring total MON metabolism In addition, the extent of triacetyloleandomycin-mediated P 450 complexes was greatly reduced by the prior addition of 100 μM MON. In DEX-treated microsomes, MON O-demethylation was found to fit monophasic Michaelis-Menten kinetics (KM = 67.6 ± 0.01 μM; Vmax = 4.75 ± 0.76 nmol/min/mg protein). Tiamulin markedly inhibited this activity in an apparent competitive manner, with a calculated Ki (Dixon plot) of 8.2 μM and an IC50 of about 25 μM. At the latter concentration, only ketoconazole or metyrapone, which can bind P 450 3A, inhibited MON O-demethylase to a greater extent than tiamulin, whereas α- **naphthoflavone**, chloramphenicol, or sulphamethasine was less effective. These results suggest that P 450 3A plays an important role in the oxidative metabolism of MON and that compds. capable of binding or inhibiting this isoenzyme could be expected to give rise to toxic interactions with the ionophore.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 20 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:245794 CAPLUS
DOCUMENT NUMBER: 129:36183
TITLE: The protein kinase c (PKC) inhibitor flavopiridol (FLAVO) significantly enhances the cytotoxic effect of chemotherapy by promoting apoptosis in gastric cancer cells
AUTHOR(S): Schwartz, G. K.; Farsi, D.; Greaney, C.; Werner, J.; Kelsen, D. K.
CORPORATE SOURCE: Department of Medicine, Division of Solid Tumor Oncology, Laboratory of Gastrointestinal Oncology, Memorial Sloan-Kettering Cancer Center, NY, USA
SOURCE: Progress in Gastric Research 1997, Proceedings of the International Gastric Cancer Congress, 2nd, Munich, Apr. 27-30, 1997 (1997), Volume 1, 627-629. Editor(s): Siewert, Joerg Ruediger; Roder, Juergen D. Monduzzi Editore: Bologna, Italy.
CODEN: 65WZAO
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The failure of many **chemotherapeutic agents** in gastric tumors reflects an inability of these drugs to induce apoptosis. Even with high concns. of paclitaxel and mitomycin-C (MMC), MKN-74 gastric cancer cells lines are resistant to the induction of apoptosis. We are able to show that flavopiridol, a synthetic **flavone**, significantly enhances the induction of apoptosis by paclitaxel and MMC in

MKN-74 treated cells.

L13 ANSWER 21 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:628243 CAPLUS
DOCUMENT NUMBER: 127:287832
TITLE: Potentiation of apoptosis by flavopiridol in mitomycin C-treated gastric and breast cancer cells
AUTHOR(S): Schwartz, Gary K.; Farsi, Kian; Maslak, Peter; Kelsen, David P.; Spriggs, David
CORPORATE SOURCE: Division of Solid Tumor Oncology, Gastrointestinal Oncology Research Laboratory, Gastrointestinal Oncology Section, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Clinical Cancer Research (1997), 3(9), 1467-1472
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Flavopiridol (L86-8275) is a synthetic **flavone** currently undergoing Phase I clin. trials. It is active against a series of human cancer cell lines and has been shown to inhibit a broad range of protein kinases, including cyclindependent kinases and protein kinase C (PKC). Previous studies have shown that the PKC-specific inhibitor safingol significantly enhances the induction of apoptosis by mitomycin-C (MMC) in gastric cancer cells. Because flavopiridol can potentially inhibit PKC, we elected to determine the extent to which flavopiridol would promote MMC-induced apoptosis in both gastric and breast cancer cells. For these studies, MKN-74 gastric cancer cells and MDA-MB-468 breast cancer cells were exposed to either no drug, 1 μg/mL MMC alone, 300 nM flavopiridol alone, or a combination of chemotherapy with flavopiridol for 24 h. Sequence specificity was also examined by first exposing cells to MMC for 24 h followed by flavopiridol for 24 h or to the same drugs in the reverse order. Apoptosis was measured by quant. fluorescence microscopy of nuclear chromatin condensation in cells stained with the dye, bisbenzimide trihydrochloride. Exposure of MKN-74 cells to flavopiridol alone induced apoptosis in 12 ± 1% of the cells, and exposure to MMC alone induced apoptosis in 10 ± 1%. However, the combination of flavopiridol and MMC increased the induction of apoptosis to 55 ± 3% of the cells ($P < 0.005$ for the drug combination vs. flavopiridol alone). Pretreatment with the PKC activator 3-phorbol 12-myristate 13-acetate only partially reversed this effect (43 ± 1%; $P < 0.025$). In MDA-MB-468 cells, flavopiridol alone induced apoptosis in 17 ± 1% of the cells, and MMC alone induced apoptosis in 10 ± 1% of the cells. The combination of flavopiridol and MMC increased the percentage of MDA-MB-468 cells undergoing apoptosis to 58 ± 4% ($P < 0.005$ for the drug combination vs. flavopiridol alone). Sequential treatment with MMC followed by flavopiridol induced apoptosis in 63 ± 2% of the MKN-74 cells ($P < 0.05$ vs. the concomitant drug combination) and in 76 ± 2% of the MDA-MB-468 cells ($P < 0.025$ vs. the concomitant drug combination), whereas flavopiridol followed by MMC did not increase the induction of apoptosis in either cell line. As determined by the terminal deoxynucleotidyl transferase labeling of the 3' ends of DNA fragments produced in apoptotic cells, the induction of apoptosis with the combination of flavopiridol and MMC occurred to MKN-74 cells in all phases of the cell cycle (i.e., G0-G1, S, and G2-M). These results indicate that flavopiridol potentiates the cytotoxic effect of the **chemotherapeutic agent** MMC by promoting drug-induced apoptosis in tumor cells. Sequencing studies suggest that MMC followed by flavopiridol or simultaneous treatment is superior to flavopiridol followed by MMC. The enhancement of MMC-induced apoptosis by flavopiridol may be partially PKC dependent and is not associated with one specific region of the cell cycle.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 22 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:561488 CAPLUS
DOCUMENT NUMBER: 127:199736
TITLE: Accelerated titration designs for phase i clinical trials in oncology
AUTHOR(S): Simon, Richard; Freidlin, Boris; Rubinstein, Larry; Arbuck, Susan G.; Collins, Jerry; Christian, Michaele C.
CORPORATE SOURCE: Division of Cancer Treatment, Diagnosis, and Centers, Cancer Therapy Evaluation Program, National Cancer Institute, Bethesda, MD, USA
SOURCE: Journal of the National Cancer Institute (1997), 89(15), 1138-1147
CODEN: JNCIEQ; ISSN: 0027-8874
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Many cancer patients in phase I clin. trials are treated at doses of chemotherapeutic agents that are below the biol. active level, thus reducing their chances for therapeutic benefit. Current phase I trials often take a long time to complete and provide little information about interpatient variability or cumulative toxicity. Our objective was to develop alternative designs for phase I trials so that fewer patients are treated at subtherapeutic dose levels, trials are of reduced duration, and important information (i.e., cumulative toxicity and maximum tolerated dose) needed to plan phase II trials is obtained. We fit a stochastic model to data from 20 phase I trials involving the study of nine different drugs. We then simulated new data from the model with the parameters estimated from the actual trials and evaluated the performance of alternative phase I designs on this simulated data. Four designs were evaluated. Design 1 was a conventional design (similar to the commonly used modified Fibonacci method) using cohorts of three to six patients, with 40% dose-step increments and no intrapatient dose escalation. Designs 2 through 4 included only one patient per cohort until one patient experienced dose-limiting toxic effects or two patients experienced grade 2 toxic effects (during their first course of treatment for designs 2 and 3 or during any course of treatment for design 4). Designs 3 and 4 used 100% dose steps during this initial accelerated phase. After the initial accelerated phase, designs 2 through 4 resorted to standard cohorts of three to six patients, with 40% dose-step increments. Designs 2 through 4 used intrapatient dose escalation if the worst toxicity is grade 0-1 in the previous course for that patient. Only three of the actual trials demonstrated cumulative toxic effects of the **chemotherapeutic** agents in patients. The average number of patients required for a phase I trial was reduced from 39.9 for design 1 to 24.4, 20.7, and 21.2 for designs 2, 3, and 4, resp. The average number of patients who would be expected to have grade 0-1 toxicity as their worst toxicity over three cycles of treatment is 23.3 for design 1, but only 7.9, 3.9, and 4.8 for designs 2, 3, and 4, resp. The average number of patients with grade 3 toxicity as their worst toxicity increases from 5.5 for design 1 to 6.2, 6.8, and 6.2 for designs 2, 3, and 4, resp. The average number of patients with grade 4 toxicity as their worst toxicity increases from 1.9 for design 1 to 3.0, 4.3, and 3.2 for designs 2, 3, and 4, resp. Accelerated titration (i.e., rapid intrapatient drug dose escalation) designs appear to effectively reduce the number of patients who are undertreated, speed the completion of phase I trials, and provide a substantial increase in the information obtained.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 23 OF 32 CAPLUS
ACCESSION NUMBER: 1997:147544 CAPLUS
DOCUMENT NUMBER: 126:180992
TITLE: Flavopiridol (L86-8275): selective antitumor activity in vitro and activity in vivo for prostate carcinoma

cells
AUTHOR(S): Drees, Markus; Dengler, Wolfgang A.; Roth, Thomas; Labonte, Heike; Mayo, Joseph; Malspeis, Louis; Grever, Michael; Sausville, Edward A.; Fiebig, Heinz H.
CORPORATE SOURCE: Department of Internal Medicine, University of Freiburg, Freiburg, D-79106, Germany
SOURCE: Clinical Cancer Research (1997), 3(2), 271-279
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have selected a panel of human tumor xenografts for in vitro and in vivo studies that allows an indication of selectivity of action of novel **chemotherapeutic agents.** We report here the antitumor activity of the **flavone** flavopiridol (previously designated L86-8275), which has been selected for further studies based in part on its behavior in the anticancer drug screening system of the United States National Cancer Institute. Eighteen human tumor and five cell line-derived xenografts established by serial passage in nude mice in our laboratory were used as tumor models for in vitro investigations using a modified double-layer soft agar assay. In vivo investigations were completed in nude mice bearing advanced-stage s.c. growing prostate cancer xenografts. Antitumor activity in vitro (test/control ≤ 30%) of flavopiridol was observed at the very low concentration of 0.1 ng/mL in three of four prostatic xenografts and in one melanoma xenograft. Overall, in 14 of 23 (61%) tumor xenografts, drug treatment resulted in a IC70 of <10 ng/mL, demonstrating the high antiproliferative potential of flavopiridol. Toxicity to in vitro bone marrow cultures was evident only at 100 ng/mL, indicating potential high selectivity for susceptible tumor cells. Comparison of tumor cells with bone marrow samples tested showed clear prostate carcinoma and moderate melanoma selectivity. In vivo studies of flavopiridol confirmed antitumor activity in both prostate cancer xenografts investigated. At the maximal tolerated dose of 10 mg/kg/day administered p.o. on days 1-4 and 7-11, flavopiridol effected tumor regression in PRXF1337 and tumor stasis lasting for 4 wk in PRXF1369. We conclude that flavopiridol shows strong prostate- and moderate melanoma-specific antitumor activity in vitro. The prostate antitumor activity is also reflected by the two in vivo models studied. Initial clin. efforts with flavopiridol might consider early evaluation in patients with prostate carcinoma.

L13 ANSWER 24 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:590815 CAPLUS
DOCUMENT NUMBER: 125:293021
TITLE: Inhibitors of NO activity for improving therapeutic effectiveness of agents for the treatment of solid tumors and other disorders
INVENTOR(S): Dewhirst, Mark W.; Meyer, Robert E.; Bonaventura, Joseph; Deangelo, Joseph
PATENT ASSIGNEE(S): Duke University, USA; Apex Bioscience, Inc.; North Carolina State University
SOURCE: U.S., 29 pp., Cont.-in-part of U.S. Ser. No. 66, 756.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5554638	A	19960910	US 1994-246882	19940520
US 5612310	A	19970318	US 1993-66756	19930524
CA 2163638	AA	19941208	CA 1994-2163638	19940523
WO 9427585	A1	19941208	WO 1994-US5791	19940523

W: CA, JP
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

EP 705098	A1	19960410	EP 1994-917468	19940523
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09500366	T2	19970114	JP 1994-500873	19940523
US 5788958	A	19980804	US 1996-709938	19960906
US 6020308	A	20000201	US 1998-126930	19980731

PRIORITY APPLN. INFO :

US 1993-66756	A2	19930524
US 1994-246882	A	19940520
WO 1994-US5791	W	19940523
US 1996-709938	A3	19960906

AB The present invention is directed to the use of an inhibitor of NO activity, such as a nitric oxide scavenger or an NO synthase inhibitor, as an antitumor therapy to reduce tumor blood flow and oxygenation. The invention is also directed to administration of a nitric oxide scavenger or a nitric oxide synthase inhibitor to enhance the effectiveness of tumor therapy with hypoxic or acidic **chemotherapeutic agents** or hyperthermia. The invention is also directed to the administration of a nitric oxide synthase substrate to a subject previously administered a nitric oxide synthase inhibitor, in order to selectively inhibit tumor perfusion. In a specific example, administration of cell-free Hb, a nitric oxide scavenger, in conjunction with mitomycin C, a hypoxic cytotoxin, results in a significant delay in tumor growth of a human tumor xenograft in a mouse compared to mitomycin C alone. In another example, the administration of an inhibitor of nitric oxide synthase followed by the administration of a substrate of the enzyme causes a specific irreversible reduction of tumor blood flow, while normal blood flow is restored.

L13 ANSWER 25 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1994:621188 CAPLUS
DOCUMENT NUMBER:	121:221188
TITLE:	Induction of multiple cytokine gene expression and IRF-1 mRNA by **flavone** acetic acid in a murine macrophage cell line
AUTHOR(S):	Eader, Lou Ann; Gusella, Luca; Dorman, Linda; Young, Howard A.
CORPORATE SOURCE:	Biological Carcinogenesis and Development Program, Natl. Cancer Inst.-Frederick Cancer Research and Dev. Center, Frederick, MD, 21702-1201, USA
SOURCE:	Cellular Immunology (1994), 157(1), 211-22 CODEN: CLIMB8; ISSN: 0008-8749
DOCUMENT TYPE:	Journal
LANGUAGE:	English

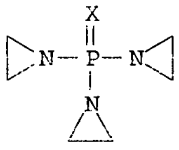
AB Flavone-8-acetic (FAA) acid is a potential **chemotherapeutic agent** that has demonstrated strong immunomodulatory activity in murine model systems. The immunomodulatory activity of this drug in murine systems has been linked to its ability to rapidly induce cytokine gene expression in vivo ad in mouse splenocytes ev vivo. We have now developed a tissue culture model for studying the mol. basis of induction of cytokine expression by FAA. Using the mouse macrophage cell line, ANA-1, we can demonstrate the direct induction of interferon β (IFNβ), interleukin-6 (IL-6), tumor necrosis factor-α (TNFα), and interferon response factor-1 (IRF-1) mRNA expression following treatment with FAA. Furthermore the induction of the IFNβ mRNA can occur in the absence of new protein synthesis. Nuclear run-on expts. indicate that at least part of the induction of IFNβ, IL-6, and TNFα mRNA occurs at the transcriptional level while the increase in IRF-1 mRNA appears largely post-transcriptional or due to the production of IFNβ protein. Addnl., expts. using agents that interfere with second messengers demonstrate that activation of the protein kinase C pathway is possibly involved in FAA gene induction. The use of this tissue culture model system should lead to a more complete understanding of the mechanisms involved in FAA-induced gene expression and help determine why this drug is inactive on human cells.

L13 ANSWER 26 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:587171 CAPLUS
DOCUMENT NUMBER: 117:187171
TITLE: Reductase and oxidase activity of rat liver cytochrome P450 with 2,3,5,6-tetramethylbenzoquinone as substrate
AUTHOR(S): Goeptar, Arnold R.; Te Koppele, Johan M.; Neve, Etienne P. A.; Vermeulen, Nico P. E.
CORPORATE SOURCE: Dep. Pharmacochem., Free Univ., Amsterdam, 1081 HV, Neth.
SOURCE: Chemico-Biological Interactions (1992), 83(3), 249-69
CODEN: CBINA8; ISSN: 0009-2797
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The main objective of the present study was to investigate the proposed role of cytochrome P 450 in the reductive metabolism of quinones as well as in the formation of reduced oxygen species in liver microsomes from phenobarbital (PB-microsomes) and β- **naphthoflavone** (βNF-microsomes) pretreated rats. In the present study, 2,3,5,6-tetramethylbenzoquinone (TMQ) was chosen as a model quinone. Anaerobic one-electron reduction of TMQ by PB-microsomes showed relatively strong ESR signals of the oxygen-centered semiquinone free radical (TMSQ), whereas these signals were hardly detectable with βNF-microsomes. Under aerobic conditions TMSQ formation was diminished and concomitant reduction of mol. oxygen occurred in PB-microsomes. Interestingly, TMQ-induced superoxide anion radicals, measured by ESR (using the spin trap 5,5'-dimethyl-1-pyrroline-N-oxide), and hydrogen peroxide generation was found to occur with βNF-microsomes as well. Furthermore, SK&F 525-A (a type I ligand inhibitor of cytochrome P 450) inhibited TMQ-induced hydrogen peroxide formation in both PB- and βNF-microsomes. However, metyrapone and imidazole (type II ligand inhibitors of cytochrome P 450) inhibited mol. oxygen reduction in βNF-microsomes and not in PB-microsomes. The present study indicates that cytochrome P 450-mediated one-electron reduction of TMQ to TMSQ and subsequent redox cycling of TMSQ with mol. oxygen constitutes the major source for superoxide anion radical and hydrogen peroxide generation in PB-microsomes (i.e. from the reductase activity of cytochrome P 450). However, most of the superoxide anion radical formed upon aerobic incubation of TMQ with βNF-microsomes originates directly from the dioxyanion-ferri-cytochrome P 450 complex (i.e. from the oxidase activity of cytochrome P 450). In conclusion, both the one-electron reduction of TMQ and mol. oxygen were found to be cytochrome P 450 dependent. Apparently, both the reductase and oxidase activities of cytochrome P 450 may be involved in the reductive cytotoxicity of **chemotherapeutic** agents containing the quinoid moiety.

L13 ANSWER 27 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:94723 CAPLUS
DOCUMENT NUMBER: 114:94723
TITLE: Combination of **flavone** acetic acid (FAA) with adriamycin, cis-platinum and difluoromethylornithine (DFMO) in vitro against human colon cancer cells
AUTHOR(S): Neelam, Sarabjit S.; Bernabei, Alvise; Freedland, Curtis; Thompson, Roxanna; Corbett, Thomas H.; Luk, Gordon D.
CORPORATE SOURCE: Sch. Med., Wayne State Univ., Detroit, MI, 48201, USA
SOURCE: Investigational New Drugs (1990), 8(3), 263-8
CODEN: INNDDK; ISSN: 0167-6997
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Unresectable solid tumors in the metastatic stage are quite resistant to current chemotherapy and radiation therapy regimens. **Flavone** acetic acid (FAA) is a novel antitumor agent which appears to work through a different mechanism than the conventional **chemotherapeutic**

agents. In preclin. studies it has been effective against a variety of transplantable murine and human tumors and appears to be solid tumor-selective. It also has nonoverlapping toxicities as compared to conventional agents. Thus, FAA was examined in vitro against human colon cancer cells and explored whether its effectiveness could be enhanced in combination with other agents such as adriamycin (ADR), cis-platinum (CP), and difluoromethylornithine (DFMO), an inhibitor of polyamine biosynthesis. Addition of FAA for 24 h in liquid media produced dose-dependent growth inhibition. Using soft agar colony assay, growth was inhibited by 58% by 3 mM FAA and only 1.4% by 0.375 mM FAA. The combination of FAA and cis-platinum produced synergism at the lower doses tested. The combination of FAA and adriamycin produced antagonism at all doses tested and the combination of FAA with DFMO did not produce results significantly different from DFMO alone. Enhancement of FAA activity can thus be achieved in combination with conventional antitumor agents, but may be drug and dose specific.

L13 ANSWER 28 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:171645 CAPLUS
DOCUMENT NUMBER: 112:171645
TITLE: Biotransformation of N,N',N"-triethylenethiophosphoramide: oxidative desulfuration to yield N,N',N"-triethylenephosphoramide associated with suicide inactivation of a phenobarbital-inducible hepatic P-450 monooxygenase
AUTHOR(S): Ng, Sze Fong; Waxman, David J.
CORPORATE SOURCE: Dana-Farber Cancer Inst., Harvard Med. Sch., Boston, MA, 02115, USA
SOURCE: Cancer Research (1990), 50(3), 464-71
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I, X=S
II, X=O

AB Oxidative metabolism of the polyfunctional alkylating agent thio-TEPA (I) was studied in isolated rat liver microsomes and purified, reconstituted cytochrome P 450 (P 450) enzyme systems in order to elucidate the pathways of drug oxidation and to identify the possible contributions of individual P 450 enzymes to the bioactivation of this **chemotherapeutic agent.** Rat liver microsomes were found to catalyze conversion of thio-TEPA to its oxo metabolite, II, in a P 450-dependent reaction that was markedly stimulated by prior in vivo treatment with drug inducers of hepatic P 450 subfamily IIB (phenobarbital), but not by pretreatment with inducers of P 450 subfamilies IA (β- **naphthoflavone**) or IIE (isoniazid). I depletion and II formation catalyzed by phenobarbital-induced liver microsomes were both inhibited by >90% by antibodies selectively reactive with P 450 PB-4 (gene product IIB1), the major phenobarbital-inducible rat liver microsomal P 450 form, but not by antibodies inhibitory toward 7 other rat hepatic P-450s. Oxidation of I to II was also catalyzed by purified P 450 PB-4 [Km (app) 19 μM; Vmax (app) = 11 mol I metbolized/min/mol P 450 PB-4] following reconstitution of the cytochrome with NADPH P 450 reductase in a lipid environment. Metabolism of I by P 450 PB-4 was associated with a suicide inactivation of the cytochrome characterized by Kinactivation = 0.096/min, KI = 24 μM, and a partition ratio of 136 mol I metabolized/mol P 450 inactivated. The metabolite, however, did not inactivate the cytochrome, nor was it subject

to further detectable metabolism In microsomal incubations, metabolism of I led to the inactivation of P 450 PB-4 (steroid 16β-hydroxylase) as well as P 450 IIIA-related enzymes (steroid 6β-hydroxylase) and the P 450-independent enzyme steroid 17β-hydroxysteroid:NADP+ 17-oxidoreductase, as demonstrated by use of the P 450 form-selective steroidal substrate androst-4-ene-3,17-dione. In contrast, little or no inactivation of microsomal P 450 IIA-related enzymes (steroid 7α-hydroxylase) or microsomal NADPH P 450 reductase was observed Substantial protection of steroid 6β-hydroxylase and steroid 17β-hydroxysteroid:NADP+ 17-oxidoreductase but not steroid 16β-hydroxylase (P 450 PB-4) was afforded by the sulfhydryl-containing nucleophiles cysteine and glutathione; this suggests that inactivation of these microsomal enzymes is mediated by diffusible, reactive metabolite(s) of I, but that in the case of P 450 PB-4, inactivation occurs before the metabolite(s) depart from the active site. These findings demonstrate that P 450 PB-4 can oxidize I to chemical reactive metabolite(s) that may potentially contribute to drug cytotoxicity.

L13 ANSWER 29 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:68875 CAPLUS
DOCUMENT NUMBER: 110:68875
TITLE: Human embryonic cell growth assay for teratogens with or without metabolic activation system using microplate
AUTHOR(S): Tsuchiya, Toshie; Matuoka, Atsuko; Sekita, Setsuko; Hisano, Takuzo; Takahashi, Atsushi; Ishidate, Motoi, Jr.
CORPORATE SOURCE: Div. Med. Chem., Natl. Inst. Hyg. Sci., Tokyo, Japan
SOURCE: Teratogenesis, Carcinogenesis, and Mutagenesis (1988), 8(5), 265-72
CODEN: TCMUD8; ISSN: 0270-3211
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In vitro microassay for the screening of teratogens was investigated on cancer **chemotherapeutic agents** sterigmatocystins and benzimidazoles using human embryonic palatal mesenchymal (HEPM) cells. Five thousand cells were inoculated into each well of 96-well microtiter plates, and cultivated for 24 h, after which the media were changed with new ones that contained various amts. of chems.; after cultivation for an addnl. 72 h, the media were discarded, and cells attached to the tissue plate were fixed and stained with Giemsa's solution; the cell number then was conducted by colony counter. For the metabolic activation, the liver S9 obtained from rats pretreated with phenobarbital and 5,6-benzoflavone and cofactors (S9 mix) were added directly to the HEPM cell cultures along with chems. After 6 h, the cultures were exchanged with a fresh medium and incubated for a further 72 h. Concns. of the cancer **chemotherapeutic agents** that inhibited growth by 50% ranged from 0.001 to 10 μg/mL. Sterigmatocystins indicated strong inhibition; among three derivs., O-acetyl sterigmatocystin was the most potent inhibitor. Benzimidazoles also exhibited an inhibitory action on HEPM cell growth; nitro and chloro groups at the 5 position in 2-(2-pyridyl)benzimidazole were potent substituents. As for the activation of cyclophosphamide in the HEPM cell culture, IC50 was decreased to 1.0 μg/mL by the incubation with S9 mix for 6 h, and sterigmatocystin was activated by S9 mix.

L13 ANSWER 30 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:13639 CAPLUS
DOCUMENT NUMBER: 110:13639
TITLE: Dental compositions containing antiphlogistic agents, antiosteoporotic agents, and local anethetics or **chemotherapeutic agents**
INVENTOR(S): Csanyi, Endre; Csanyi, Gabor; Balogh, Tibor; Nagy, Laszlo

PATENT ASSIGNEE(S): Reanal Finomvegyszergyar, Hung.
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8805650	A1	19880811	WO 1988-HU3	19880129
W: AU, DK, JP, KR, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
HU 201474	B	19901128	HU 1987-360	19870203
AU 8812263	A1	19880824	AU 1988-12263	19880129
EP 349535	A1	19900110	EP 1988-901085	19880129
EP 349535	B1	19920108		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 02502375	T2	19900802	JP 1988-501316	19880129
JP 07096486	B4	19951018		
AT 71276	E	19920115	AT 1988-901085	19880129
CN 88100498	A	19880928	CN 1988-100498	19880203
DD 273977	A5	19891206	DD 1988-312633	19880203
CS 277001	B6	19921118	CS 1988-674	19880203
CA 1327529	A1	19940308	CA 1988-558061	19880203
ES 2009561	A6	19891001	ES 1988-675	19880307
DK 8805431	A	19880929	DK 1988-5431	19880929

PRIORITY APPLN. INFO.:

HU 1987-360	A	19870203
EP 1988-901085	A	19880129
WO 1988-HU3	A	19880129

AB A dental comp., useful as a therapeutic dental filling for preserving teeth during any stage of pulpitis and periodontitis , comprises an antiosteoporotic agent, an antiphlogistic agent, an optional natural or synthetic **chemotherapeutic agent** or local anesthetic, and ≥1 known auxiliary agents. A mixture containing doxycycline hyclate 2, triamcinolone 0.8, **ipriflavone** 2.0, ZnO 80, and CaO 15.2 g, was admixed with eugenol to obtain a therapeutic dental cement.

L13 ANSWER 31 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:161016 CAPLUS
DOCUMENT NUMBER: 108:161016
TITLE: The structure of **flavone**-8-acetic acid, a **chemotherapeutic agent**, and its application to drug design
AUTHOR(S): Rabinovitz, M.
CORPORATE SOURCE: Div. Cancer Treat., Natl. Cancer Inst., Bethesda, MD, 20892, USA
SOURCE: Journal of Enzyme Inhibition (1988), 2(2), 151-2
CODEN: ENINEG; ISSN: 8755-5093
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pyrone-2-propionic acid may be the active moiety of the resonance form of **flavone**-8-acetic acid, an agent with high activity against colon adenocarcinoma.

L13 ANSWER 32 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1949:768 CAPLUS
DOCUMENT NUMBER: 43:768
ORIGINAL REFERENCE NO.: 43:224f-i,225a-i,226a-i
TITLE: Basically substituted xanthone and thiaxanthone derivatives; miracil, a new **chemotherapeutic agent**
AUTHOR(S): Mauss, Hans
SOURCE: Chemische Berichte (1948), 81, 19-31
CODEN: CHBEAM; ISSN: 0009-2940

DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB cf. Naturwissenschaften 33, 253(1946). It seemed likely that the preparation of soluble salts of basically-alkylated xanthone derivs., like plasmochin in the quinoline and atebrin in the acridine series, would lead to interesting results. Basically substituted ethers and carboxamides of xanthone (I) showed no chemotherapeutic activity, but replacement of a Cl atom or other reactive substituent adjacent to the CO group by basic residues yielded compds. which in animal expts. gave indication of activity against the causative agents of bilharziasis (schistosomiasis). In what follows, R = 2-diethylaminoethylamino. 1-R-xanthone (II) showed no activity against schistosomes, and it was found that a Me group in the para position to the basic group is essential for activity. Replacement of this Me group by Et, MeO, or even Cl again results in loss of activity, whereas in the atebrin series Cl and Me are mutually replaceable without affecting the activity. Furthermore, in the I series, the activity in general decreased when the number of C atoms in the basic side chain exceeded 2. Starting with a short basic chain and a Me group in the para position to it [1-R-4-methylxanthone, miracil A (IIa)], attempts were made to increase the activity by suitable substitution. This was effected by introduction on the unsubstituted benzene of Me, MeO, or Cl, a 6- proving to be therapeutically more effective than a 7-substituent. In this series 6-chloro-1-R-4-methylxanthone (miracil B) (III) was the most active in the mouse test, but all, except IIa, were inactive (possibly because of poor resorption) against bilharziasis in the ape. Further attempts to obtain more active and more easily resorbable derivs. led to 1-R-4-methylxanthydrol (miracil C) (IV), which was more effective both in the mouse and in the ape test. Quaternary basic xanthone salts proved to be inactive. On the other hand, 1-R-4-methylthiaxanthone-HCl (miracil D) (V) was the most effective in the ape test of any compound thus far prepared Variation of the basic group resulted in loss of activity except in the case of the Et2N(CH2)3NH derivative Derivs. of V with a 2nd Me group on the substituted benzene ring or a Cl atom on the other benzene ring retained their activity but replacement of the 4-Me group by MeO or Cl resulted in inactive compds. The sulfone of V was inactive, while the thiaxanthene and its analogs were active. V is to be tested clin. II, yellow crystals from ligroin, m. 99-100°, was obtained from 22.6 g. 1-methoxyxanthone and 35 g. Et2NCH2CH2NH2 heated 5 h. at 190-200°, together with a considerable amount of 1-hydroxyxanthone. o-(5-Chloro-2-methylphenoxy)benzoic acid, m. 117-18° (from alc.), was obtained in almost 90% yield from o-ClC6H4CO2H and 5,2-ClMeC6H3OH according to Ullmann and Zlokasoff [Ber. 38, 2111(1905)]; heated on the water bath with concentrated H2SO4, it gave about 85% 1-chloro-4-methylxanthone (VI), m. 133-4° (from alc.). VI boiled 10 h. in PhNO2 with 1.5 mols. p-MeC6H4SO2NH2, KOAc, and a little Cu bronze, and the resulting 1-sulfonamido compound gently heated 1 h. on the water bath with concentrated H2SO4, yielded about 85% 1-amino-4-methylxanthone (VII), deep yellow crystals from alc., m. 139-40° [Ac derivative, m. 175-6° (from alc.)]. 1-(Methylamino) compound, from VI and alc. MeNH2 heated several hrs. at 180-90°, yellow crystals from benzene-ligroin (1:2), m. 133-4°. 1-(2-Hydroxyethylamino) compound (about 90% from VI and HOCH2CH2NH2 heated several hrs. at 170° with pyridine and Cu bronze), yellow, m. 187-8° (from alc.), gives on heating 2 h. on the water bath with excess POCl3 about 60% of the 1-(2-chloroethylamino) compound (VIII), yellow needles from alc., m. 145-6°. 1-R compound (IX) (around 90% from VI and Et2NCH2CH2NH2 heated 6 h. at 170°), yellow crystals from alc., m. 76-7°; HCl salt, yellow, m. 190-1°; picrate, reddish yellow crystalline powder from alc., m. 136-7°. IX is also obtained from VII slowly heated (0.5 h.) to 150° with 1.1 mols. Et2NCH2CH2Cl; from VIII heated 6 h. at 190° with excess Et2NH in toluene; and in moderate yield by ring closure of o-(2,5-MeRC6H3O)C6H4CO2H with concentrated H2SO4. 4-R-2-hydroxytoluene, b4 178-9°, obtained by demethylation of the Me ether, b3 154-5°, with concentrated HBr. IX heated 4 h. at 170-80° with alc. KOH, the alc. driven off, water added, and the

alkaline solution extracted with ether and acidified with dilute HCl yields an amphoteric precipitate redissolving in excess of acid; taken up in ether and purified through the AcOH salt, it gives 6-R-2,2'-dihydroxy-3-methylbenzophenone (X), yellow crystalline powder from alc., m. 88-9° [picrate, yellow, m. 177-8° (from alc.)]; during the purification of X through the AcOH salt there is obtained, as an acid-insol. byproduct, a small amount of 1-hydroxy-2-methylxanthone, yellow needles from alc., m. 148-9°, formed in larger yield when X is boiled a short time in AcOH and allowed to cool; the 2 xanthones are formed in the ratio 4:5 in this condensation. o-(5-Chloro-2,4-dimethylphenoxy)benzoic acid, from o-ClC6H4CO2H and 5,2,4-ClMe2C6H2OH, m. 146-7° [from dilute alc. (4:1)], converted by concentrated H2SO4 into 1-chloro-2,4-dimethylxanthone, m. 159-60°; 1-R-2,4-dimethylxanthone-HCl, yellow, m. 179-80° (from alc.). 4-Chloro-2-(5-chloro-2-methylphenoxy)benzoic acid (about 70% from 2,4-Cl2C6H3CO2H and 5,2-ClMeC6H3OH), m. 176-7° (from alc.); 1,6-dichloro-4-methylxanthone (yield almost quant.), m. 177-8° (from glacial AcOH), gives with Et2NCH2CH2NH2 the 1-R compound, yellow, m. 87-8° (from ligroin) [HCl salt, yellow, m. 255-6° (decomposition); methanesulfonate, yellow, m. 142-3°]. 5-Chloro-2-(5-chloro-2-methylphenoxy)benzoic acid, yellowish, m. 177-8° (from alc.); 1,7-dichloro-4-methylxanthone, m. 198° (from glacial AcOH); 1-R compound, isolated in about 80% yield as the HCl salt, yellow, m. 243° (from alc.). 2-(5-Chloro-2-methylphenoxy)-4-methylbenzoic acid, m. 138-9° (from alc.); 1-chloro-4,6-dimethylxanthone, needles from alc., m. 168°; 1-R compound [about 75% as the HCl salt, yellow, m. 217-18° (from alc.)]. 2-(5-Chloro-2-methylphenoxy)-5-methylbenzoic acid, m. 173-4° (from alc.); 1-chloro-4,7-dimethylxanthone, m. 152° (from alc.); 1-R compound [HCl salt, yellow, m. 198° (from alc.)]. 2-(5-Chloro-2-methylphenoxy)-4-methoxybenzoic acid, m. 174-5° (from alc.); 1-chloro-6-methoxy-4-methylxanthone, needles from glacial AcOH, m. 176-7°, greatly depresses the m.p. of the 7-MeO derivative below; 1-R compound yellow, m. 84-5° (from ligroin), isolated as the yellow HCl salt, m. 225-6° (decomposition) (from alc.). 2-(5-Chloro-2-methylphenoxy)-5-methoxybenzoic acid m. 183° (from alc.); 1-chloro-7-methoxy-4-methylxanthone m. 175-6° (from alc.); 1-R compound [HCl salt, yellow, m. 189-90° (from alc.)]. IV, from the xanthone in boiling aqueous alc. NaOH with Zn dust, needles from ligroin (b. 60-70°), m. 100°, forms on cautious neutralization with dilute HCl a yellow solution which with a slight excess of acid becomes deep blue-green. o-HSC6H4CO2H and p-ClC6H4Me with concentrated H2SO4 give a mixture of 1-chloro-4-methyl- (XI) and 4-chloro-1-methylthiaxanthone (XII) which can hardly be separated (Ullmann and v. Glenck, C.A. 11, 2668). Only the Cl atom of XI reacts with Et2NCH2CH2NH2, and when 39 g. of the mixture of XI and XII was heated 4 h. with an excess (54 g.) of the amine, treated with 100 cc. of 2 N NaOH, distilled with steam, the NaOH solution decanted off, the semisolid residue treated with 10% AcOH, and the insol. unchanged XII, m. 141-2°, filtered off, NH4OH or dilute NaOH precipitated from the orange-red filtrate about 22 g. of the free base of V, yellow, m. 64-5° (from alc.); HCl salt (V), yellow, m. 195-6°, soluble in water with orange-yellow color and neutral reaction. The base is also obtained from 1-amino-4-methylthiaxanthone and 1.1 mols. Et2NCH2CH2Cl heated 1 h. at 150°. 1-Acetamido-4-methylthiaxanthone, yellow needles from benzene, m. 180-1°; 1-(2-hydroxyethylamino) compound (about 60% from the mixture of XI and XII with H2NCH2CH2OH), orange needles (from alc.), m. 183-4°, gives with POCl3 the 1-(2-chloroethylamino) compound, yellow, m. 146° (from alc.), converted by Et2NH into V. 1-(3-Diethylaminopropyl) analog of V, from the mixed XI and XII with Et2N(CH2)3NH2 (b16 59-61°), orange-red oil; HCl salt, yellow, m. 173°. 1-Chloro-2,4-dimethylthiaxanthone, from o-HSC6H4CO2H and 2,4-Me2C6H3Cl, fallow, m. 143-4° (from glacial AcOH); 1-R compound, orange-yellow, m. 193-4° (from MeOH-Et2O). 1-R-4-methoxythiaxanthone, from the 1-Cl compound, isolated in small yield

as the orange HCl salt, m. 246-8°. 1,6-Dichloro-4-methylthiaxanthone (XIII), obtained mixed with the 4,6-dichloro-1-Me isomer (XIV) from 4,2-Cl(HS)C6H3CO2H and p-ClC6H4Me, needles from glacial AcOH, m. 182-3°; 1-R compound, from the mixture of XIII and XIV, red oil soon solidifying and separating from alc. in yellow crystals, m. 96-7° [HCl salt, yellow, m. 246-7° (from glacial AcOH), difficultly soluble in cold, more easily soluble in hot water with an orange-yellow color]. The residue remaining after extracting the base with dilute AcOH yields from glacial AcOH yellowish crystals of XIV, m. 201°. The mixture (130 g.) of XI and XII stirred 4 h. in 1300 cc. glacial AcOH with 300 cc. of 25% H2O2, let stand overnight, heated 6 h. at 50-60°, and cooled, yields 114 g. of a mixture, m. 177.5°, of the mixed sulfones, which, heated 6 h. at 170-80° with Et2NCH2CH2NH2 and pyridine, gives 1-R-4-methylthiaxanthone 10-dioxide, orange needles from alc., m. 116-17°, isolated as the HCl salt, orange-yellow, m. 230° (from MeOH); the alc. mother liquors from the salt yield the yellow HCl salt, m. 220° (from MeOH), of the 4-R-1-Me dioxide (XV), yellow scales from alc., m. 128-9°. 4-Chloro-1-methylthiaxanthone 10-dioxide (51 g. from 52 g. of the thiaxanthone, m. 141-2°, with H2O2 in glacial AcOH), yellowish white, m. 170-1°, gives XV with Et2NCH2CH2NH2 and Cu bronze in pyridine at 170-5°. 1-R-4-methylthiaxanthene (XVI), from the xanthone in boiling alc. gradually treated with Na, fallow, m. 66-7° (from alc.); HCl salt, m. 142-3°. 1-Amino-4-methylthiaxanthene, prisms from alc., m. 96-7° [Ac derivative, m. 195-6° (from alc.)], gives XVI with Et2NCH2CH2Cl at 150°.

=> logoff
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	140.36	150.43

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-25.55	-25.55

STN INTERNATIONAL LOGOFF AT 16:13:27 ON 21 MAR 2005